
Yeshiva University
UNDERGRADUATE RESEARCH ABSTRACTS
Volume 5 / 2011-2012
A Publication of Yeshiva College and Stern College for Women
A Journal of Undergraduate Research

UNDERGRADUATE RESEA

Undergraduate Research Abstracts Journal A Publication of Yeshiva College and Stern College for Women
Volume 5 : 2011-12

RCH ABSTRACTS. *Dedication*

In Tribute to our friends and mentors,

Eli Steinberger z'l

(USRP Co-President 2006-07)

&

Donny Ladell z'l

(USRP Co-President 2005-06)

Whose vision of undergraduate participation in scientific research still influences the growing, vibrant science community at Yeshiva University.

Eli and Donny, your passion for Torah and science will always inspire us. As the years pass since you left us, we continue to miss you dearly.

Staff

Yeshiva University

Undergraduate Research Abstracts Journal A Publication of
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Preface

I am delighted to present to the Yeshiva University Community the 2012 issue of the Undergraduate Research Abstracts Journal. This issue continues our annual tradition to report on the exciting research results obtained by students of Stern College for Women and Yeshiva College in different scientific disciplines.

It is the excitement and the curiosity about science that are tell-all signs of a future researcher. For Yeshiva students, they are matched with excellent opportunities on campus and elsewhere, created by our faculty, administration and their colleagues in US and abroad. As a result, our students thrive in a culture where it is not uncommon for freshmen to spend summers in world leading research laboratories, co-author research articles, and deliver presentations at international science conferences. I am most impressed how well they acquire one of the most difficult skills to learn: to be a leader and a team player at the same time. The fact that the editors have put together such an impressive record of achievements done across the campuses and academic disciplines, and have done so in a way that highlights the pride in our University as a place to do science, is a testament to the success of both their cross-campus partnership and individual leadership skills!

This Publication provides a snapshot of the first class research done in those fields of science that address the most important needs of our society: from the studies of health effects of novel nanomaterials, to the search of treatment for cancer and AIDS, to solving challenging physical and engineering problems at the nanoscale. As science and technology of the 21st century evolves to adapt to the new economical and political realities in the world, such training will some day be required not only for future scientists, but for future entrepreneurs and policy makers as well. In the mean time, it is with great joy I applaud our students for their dedication and accomplishments, and I also thank their mentors, on behalf of the YU science community.

Anatoly I. Frenkel

Professor and co-Chair, Physics Department
Chair, Department of Natural Sciences and Mathematics,
Yeshiva University

Introduction

The Undergraduate Research Abstracts Publication embodies the scientific achievements of the undergraduate campuses of Yeshiva University: Yeshiva College and Stern College. Yeshiva University offers many vibrant science clubs, thanks to the many dedicated student leaders on campus. Computer Science, Chemistry, Biology, Physics, and Neuroscience are among the science clubs on both undergraduate campuses. These clubs provide scientific events for the YU student body, and they have enthusiastically connected to local high schools and elementary schools to teach science. Moreover, the annual Medical Ethics Conference exemplifies the unity at Yeshiva University by engaging students, faculty and alumni in groundbreaking ethical dilemmas that relate to scientific discoveries.

The students, faculty, and alumni of Yeshiva University share not only their pursuit of knowledge but also in their scientific achievements. The faculty at Stern College and Yeshiva College has won awards and grants that fund millions of dollars in scientific research at the University. Bonds made between students and faculty members who conduct research together continue on, even after graduation. Graduates from Yeshiva University pursue diverse scientific interests in graduate schools, including dentistry, medicine, optometry, research, engineering and public health programs. The science departments at both YC and Stern have grown significantly over the years, and are enormous sources of pride to the university.

Student research is conducted at YU in many different scientific fields. From quantum mechanics to respiratory physiology, this publication is testament to the wide range of scientific topics that the undergraduate students and faculty of Yeshiva University take interest in. Undergraduate students have the opportunity to collaborate with scientists in other top institutions through various summer research programs such as the Roth Institute Scholars Program in Biomedical Research at Albert Einstein College of Medicine of Yeshiva University and the YU Research Internship at Bar-Ilan University in Ramat Gan, Israel. These programs focus not only on the independent research that students perform, but also on exposing students to the role that scientific research has in advancing an institution, or an entire country.

Yeshiva University represents the fusion of Torah U'Maddah, the commitment to a set of Jewish ideals and values in conjunction with academic learning and achievements. Rav Soloveitchik explains that G-d brought Adam into this world to "Fill the land and conquer it" (Genisis 1:28), to be ambitious and engage his curiosity about G-d's world by finding out how this world works. Adam was created not only to serve G-d, but to engage in scientific research. The students of Yeshiva University are committed to the dual goal of both serving G-d and researching His world, to attempt to better it.

Without further ado, the Undergraduate Research Abstracts Publication brings to you an enlightening synthesis of cutting edge research performed by the women and men of Yeshiva University. We thank the authors for their hard work and commitment to this worthy project. Without them, this publication would have never come to fruition.

To express only an atom of our appreciation to our faculty advisors, we would like to thank Dean Karen Bacon, Dr. Anatoly Frenkel, Dr. Harvey Babich and Dr. Alyssa Schuck who helped make this publication a reality.

Geulah Ben-David
Daniel Alweis
Gilad Barach
Faygel Beren
Menachem Spira
Samantha Selesny
Bella Wolf

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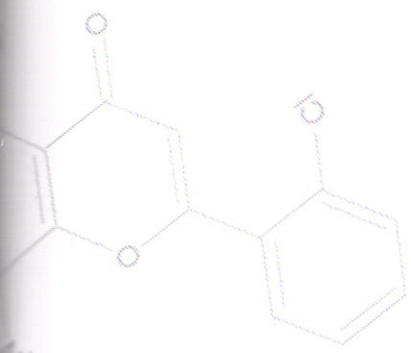

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Measuring Effects of p53 Mutations on DNA Binding with Microfluidic Affinity Analysis

by

Rachel Blinick[1], Dorit Avrahami[2], and Doron Gerber[2]

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P53 is a tumor suppressor protein that is encoded by the gene *TP53* and is made up of 393 amino acids. The protein is known to act as a tumor suppressor by inducing cell cycle arrest, activating DNA repair proteins and facilitating apoptosis for the damaged cell that cannot undergo rescue. The wildtype p53 is known to prevent tumor growth whereas mutated p53 proteins are common in many types of cancer. Current theory suggests that mutated p53 interferes with the wildtype through a negative dominant effect, but this theory does not always seem to hold true. The objective of the current study is to compare p53 and its corresponding mutants' DNA binding preferences and to investigate whether a change in DNA binding preferences can explain some of the discrepancies in the literature.

To this end, the mutations Q165P, R273H, R175H, and R248W were introduced into p53 by point directed mutagenesis and verified by sequencing. Mutant p53 plasmids were transformed into XL 10-Gold ultracompetent bacterial cells. Promoters and terminators were then added to the p53 DNA sequences by assembly PCR, creating a synthetic gene. These genes were expressed with rabbit reticulocyte lysate, producing the mutated p53 proteins.

For DNA binding analysis, the lab is currently employing the use of a microfluidics device (Figure 1) that enables up to 10,000 assays to be performed at once. The device is made up of two layers: the flow layer and the control layer. The flow layer is made up of the DNA chamber and protein chamber, while the control layer is made up of the neck valve, sandwich valve, and button valve. Once activated, the valves enable researchers to control the flow layer. The neck valve separates between the DNA and protein chambers; the sandwich valve separates between protein chambers; and the button valve enables researchers to pull down the protein and trap interactions.

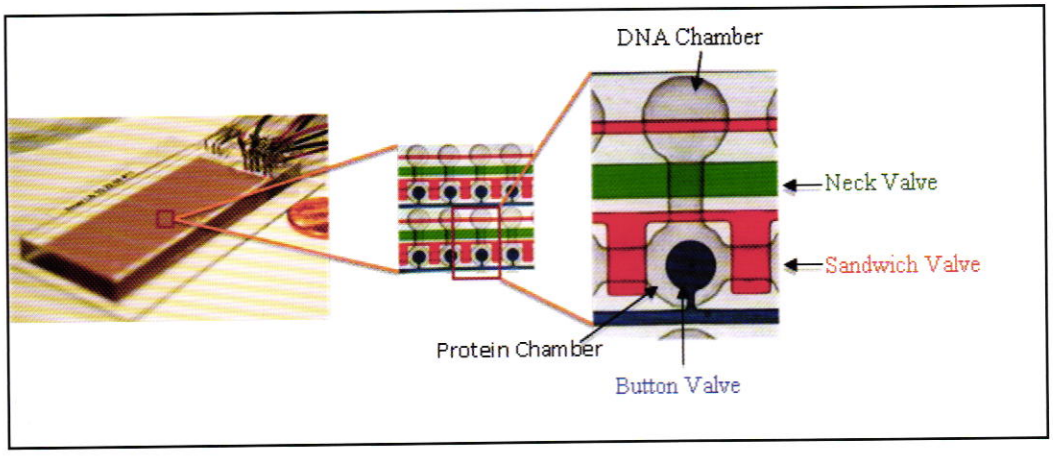

Figure 1. Microfluidic device for measuring DNA-protein interactions

To use the microfluidics device, a DNA microarray is aligned with the device so that each DNA spot lies within a DNA chamber. After performing surface chemistry in the protein chamber to enable pull down of the protein, the protein is flowed into the protein chamber with the neck valve closed. Once the protein is pulled down in each chamber, the sandwich valves are closed and the neck valves are opened to allow the DNA to diffuse into the protein chamber and bind to the protein, in this case either p53 or one of its mutants.

Combining a DNA microarray with the microfluidics assay allows us to screen p53 for interactions with a huge spectrum of DNA sequences. Based on this data, we hope to identify the effects of these mutations on protein-DNA binding and ultimately, DNA transcription.

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Student Researcher
Rachel Blinick is a senior at Stern College majoring in Biology and is co-president of the Medical Ethics Society of the Undergraduate Yeshiva University. Currently involved in biomedical research laboratory studies at Stern College and having conducted research at Bar Ilan University this past summer, Rachel is very passionate about the biomedical research world. In her spare time, she enjoys reading, tobogganing and discussing medical ethics with peers and mentors.
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Cancer Biology

Antiproliferative and Pro-Apoptotic Properties of Ellagic Acid to Oral Carcinoma HSC-2 Cells

by

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There is a growing interest in natural phytocompounds for cancer prevention and possible treatment. Ellagic acid ($C_{14}H_6O_8$) is a simple polyphenol present in fruits, such as pomegranate, and in berries, such as strawberry, raspberry, and blackberry. *In vitro* studies with mammalian cells in culture have demonstrated that ellagic acid has antiproliferative and pro-apoptotic effects on cancerous cells derived from the skin, esophagus, pancreas, colon, breast, prostate, and neural tissues. However, the effects of ellagic acid on cancer cells from the human oral cavity have not, as yet, been studied. Thus, the target cells used in research herein were human oral carcinoma HSC-2 cells.

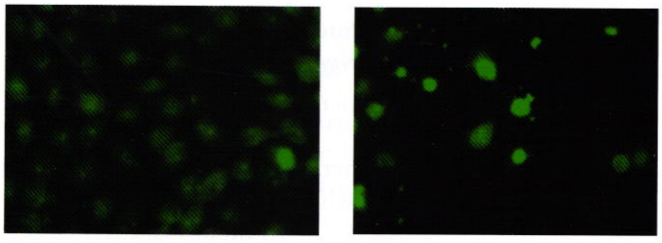
Ellagic acid, at a concentration range from 25 to 200 μM, did not affect the viability of HSC-2 cells during a 24-hr exposure. Toxicity was noted, however, for longer exposures, with a midpoint toxicity value slightly greater than 200 μM for a 2-day exposure and at 125 μM for a 3-day exposure. As shown by brightfield microscopy for a 2-day exposure of cells treated with ellagic acid and subsequently stained with aceto-orcein, increasing the concentration of ellagic acid increased the occurrence of cytopathologies, as noted by decreased cell numbers and by cells with diffuse cytoplasm and condensed nuclei.

Ellagic acid caused cell death by apoptosis, as seen by fluorescence microscopic examination of cells treated with ellagic acid and stained with acridine orange. As the concentration of ellagic acid was progressively increased for a 2-day exposure, the numbers of cells exhibiting hypercondensed nuclei, blebbing, and apoptotic bodies increased (Figure 1). Biochemical indicators of apoptosis were studied by immunoblot analysis of specific apoptosis marker proteins. Caspase-3 is a key executioner of apoptosis; its activation is indicated by cleavage of the pro-enzyme at aspartic acid 175, yielding 17/19 kD and 12 kD active products. Immunoblot analyses of cell lysates treated with 100, 175, and 200 μM ellagic acid for 2 days showed activation of caspase-3 protein. Another marker of irreversible apoptotic cell death is the cleavage, and thereby inactivation, of poly(ADP-ribose) polymerase (PARP) by caspase enzymes. PARP cleavage products were detected in protein lysates of cells exposed for 2 days to 100, 175, and 200 μM ellagic acid, but not in untreated cells (Figure 2).

Polyphenols can act both as antioxidants and as pro-oxidants. The FOX assay was used to quantify the generation of hydrogen peroxide in cell culture medium amended with ellagic acid. Although hydrogen peroxide was detected, the amounts were minimal. These data supported the finding that pyruvate, a scavenger of hydrogen peroxide (pyruvate + hydrogen peroxide → acetate + carbon dioxide + water) did not protect the cells against exposure to ellagic acid. Apparently, the levels of hydrogen peroxide that were generated were insufficient to evoke a cytotoxic response.

However, there was some indication that ellagic acid acted as an antioxidant. The diacetate ester of 2', 7'-dichlorodihydrofluorescein (DCHF-DA) is a colorless, nonfluorescent, nonpolar molecule that passively diffuses into cells and is used to detect intracellular hydrogen peroxide. Within the cell, esterases cleave the two acetates to form DCHF, a nonpermeable, polar molecule. Oxidation of the trapped non-fluorescent DCHF yields the fluorescent product, 2'7'-dichlorofluorescein, which can be visualized by a fluorescence microscope. Minimal fluorescence was observed in HSC-2 cells, both control and those exposed to 33.1 μM ellagic acid for 4 hr, whereas cells exposed to 200 μM hydrogen peroxide for 4 hr fluoresced brightly. Intracellular fluorescence was not observed in HSC-2 cells co-exposed to ellagic acid + hydrogen peroxide, thus indicating the antioxidant property of ellagic acid.

Ellagic acid was a potent inducer of apoptosis and inhibited proliferation of oral carcinoma cells. These studies suggest that consumption of ellagic acid-containing fruits and berries may play a role in cancer prevention in the oral cavity.



(a) (b)

Figure 1. HSC-2 cells: (a) Untreated control; (b) Cells treated with 175 μM ellagic acid; apoptotic bodies indicated by arrowhead. Acridine orange stain; magnification 320X.

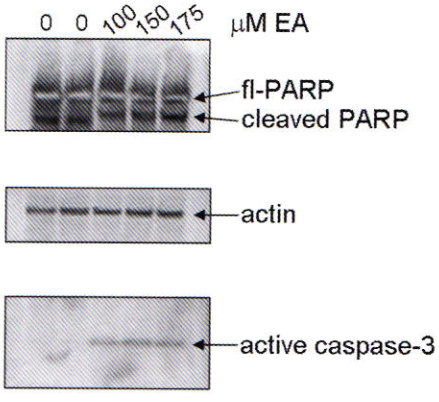


Figure 2. Immunoblot analysis of PARP cleavage (top panel) and caspase-3 activation (bottom panel) in HSC-2 cells untreated and exposed to increasing concentrations of ellagic acid for 48 hr. Actin levels were detected as a loading control (center panel).

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Student Researchers

Simone Fertel is from New Orleans, Louisiana and is a Biochemistry major at Stern College. Upon graduation in Spring 2013, Simone plans to attend medical school. Currently volunteering in NYU's Fertility Center, Simone plans on specializing in fertility medicine one day. Simone also enjoys playing basketball in her free time and advoacting on behalf of breast cancer awareness as the head of Stern's Sharsheret chapter.

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Sarah Reiss is a junior at Stern College for Women. She is majoring in Biology and plans to graduate in May 2013.

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Cancer Biology

Elucidating the Regulation of Myosin-IIA Heavy-Chain Phosphorylation by GPCRs

by

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Cancer becomes truly dangerous at the point of metastasis – when cancer cells migrate to distant portions of the body and generate new colonies. Chemotaxis, the migration of cells in response to chemical stimuli, is thought to play a significant role in metastasis. Cytoskeletal rearrangement after stimulation has been somewhat characterized. The main elements are protrusion of a lamellipodium at the anterior end of the cell and retraction of the posterior end. Nevertheless, the underlying mechanisms are not well understood. It is known, however, that contractile forces are necessary for this activity, and type II myosin supplies force by pulling on f-actin stress fibers. It has been demonstrated that when a cell is stimulated by EGF, the heavy chain of non-muscle myosin-IIA (MIIA-HC) is transiently phosphorylated at S1943 in a PI3K-dependent manner (as evidenced by lack of phosphorylation in the presence of the PI3K inhibitor wortmannin). This phosphorylation inhibits myosin-IIA filament assembly, allowing breakdown of myosin-IIA filaments and movement of myosin-IIA monomers toward new adhesion sites. We used MDA-MB-231 carcinoma cells to test for similar phosphorylation in response to LPA, which signals through GPCRs. Cells were quiesced, stimulated with 10μM LPA, and lysed at time points between 0 and 10 minutes. Levels of total and phosphorylated myosin were examined by Western blotting and compared to determine phosphorylation at each time point. A transient increase in phosphorylated MIIA-HC was observed, although further repetitions will be needed to verify statistical significance. Once this phenomenon is confirmed, the role of PI3Ks in LPA-induced MIIA phosphorylation can be examined by blocking production of PI3Ks with shRNA.

This work was supported by the Roth Scholars program and Grant 1P01 CA100324-09.

Student Researcher

A Garden State native, Ariel Caplan has risen through the ranks to become a super-senior at Yeshiva College, majoring in Biology. He enjoys investigating and writing about the interplay between biology and Jewish law and thought. He also composes poetry and satire.

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Cancer Biology

Rapamycin as an Important Therapeutic Agent in Breast Cancer Treatments

by

Naamah N. Plotzker, Jonathan Maik, Davita Wachsstock, Miriam Maruani, and Marina K. Holz, Ph.D.

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Breast cancer cell proliferation is caused in part by gene expression mediated by estrogen receptor α (ERα). ERα is activated by the phosphorylation of Serine-167 by the enzyme S6 kinase 1 (S6K1). Because breast cancer cell proliferation is often facilitated by ERα/estrogen, breast cancer is usually treated by anti-estrogen therapy. However, this treatment is not always effective since there exist estrogen-independent pathways of ERα activation. One pathway, called the MEK pathway and inhibited by the drug U0126, is activated by serum growth factors. The second pathway responsive to growth factors, insulin, and nutrients, is called the mTOR pathway which activates S6K1. A drug, rapamycin, has been found to inhibit mTOR, and thus S6K1, preventing breast cancer cell proliferation. Our lab experiments sought to demonstrate how rapamycin in concert with the drugs that inhibit the estrogen-dependent pathways and the serum-induced pathway, is more effective in preventing breast-cancer cell proliferation than anti-estrogen therapy alone. Our research is within the realm of the personalized medicine approach, which aims to treat cancer through the determination of specialized drug regiments that block active cellular pathways unique to an individual's cancer.

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Acknowledgement

Naamah, Davita, and Jonathan would like to thank Professor Marina Holz for the opportunity to work in her lab and for all of her guidance.

Student Researchers

Naamah Plotzker is a junior majoring in Biology with a very typical life, so she hopes to defy stereotypes in ways other than her personal history. She is extremely grateful to her parents for giving her the opportunity to get a great education at Stern, an experience she is enjoying immensely. Naamah is very involved with extracurricular activities at Stern College including *The Observer*, the Drama Society and Recyclemania.
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Davita Wachsstock hails from the wild, wild, Midwest. Davita is currently a sophomore at Stern College pursuing a degree in Molecular and Cellular Biology. An energetic research assistant in the lab of Dr. Holz, Davita looks forward to maximizing her science education at Stern College. When not getting carried away with molecular biology, Davita enjoys attending Jewish history classes, culturing microorganisms, and composing major symphonies.
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Jonathan Maik is a junior majoring in Biology at Yeshiva College from Livingston New Jersey. Jonathan is the President of the Yeshiva University Public Health Club and is currently involved in Emergency Medicine Research. He is especially appreciative to his parents who always support his endeavors.
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Cancer Biology

The Proapoptotic Effects of Ellagic Acid, a Metabolite of Pomegranate Extract, on Human Oral Carcinoma HSC-2 Cells

by

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Previous work in our laboratory has shown that pomegranate extract behaves as a pro-oxidant, generating hydrogen peroxide in cell culture media, and inducing oxidative stress in target cells. The purpose of this study was to evaluate whether the pro-oxidant behavior observed with pomegranate extract was due, in part, to ellagic acid, a metabolite produced when pomegranate extract is hydrolyzed. Our laboratory demonstrated that human oral carcinoma HSC-2 cells treated with increasing concentrations of ellagic acid were killed in a dose dependent manner. This cytotoxic behavior was not due to oxidative stress, as no observations of a reduction in intracellular glutathione levels, a hallmark of oxidative stress, were seen.

Flow cytometric analyses of HSC-2 cells untreated and treated with increasing concentrations of ellagic acid showed that with increasing dosages of ellagic acid, number of viable cells decreased while the number of apoptotic and non-viable cells increased (Figure 1).

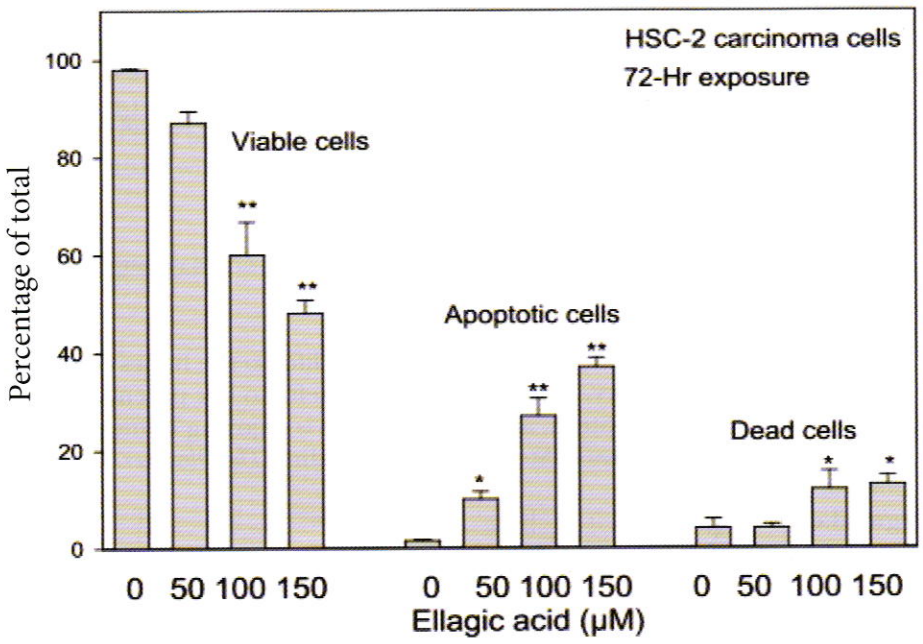

Figure 1. Proapoptotic inducing ability of ellagic acid to HSC-2 cells. Percentage of viable, apoptotic, and dead cells were measured after a 72 hr exposure to ellagic acid. Data are expressed as the arithmetic mean percent of control ± S.E.M. *P ≤ 0.01; **P≤0.05.

Increasing dosages of ellagic acid correlated with activation of the apoptotic-inducing enzymes, caspase 3 and caspase 7 (Figure 2).

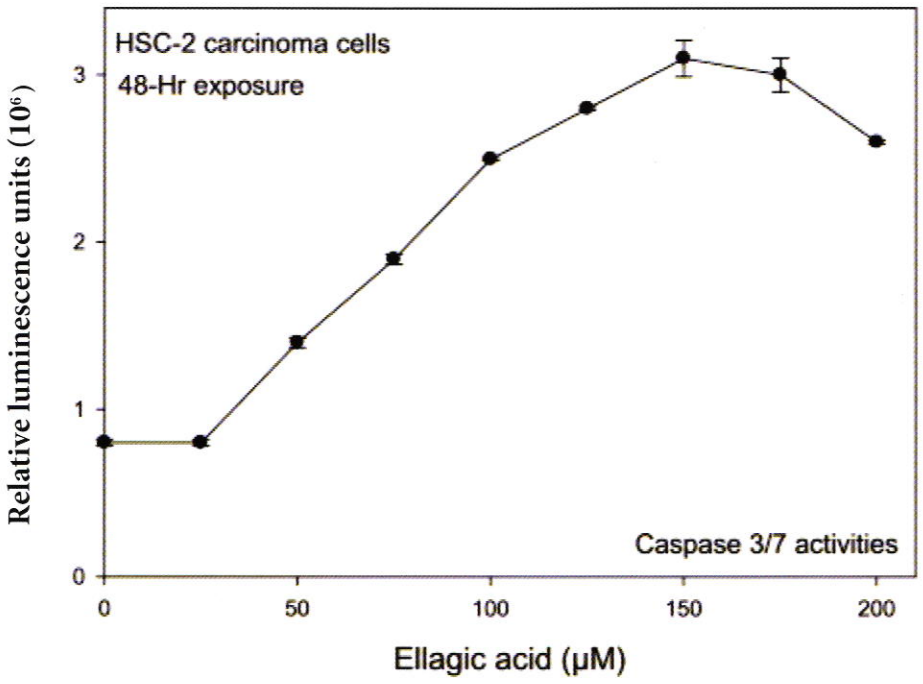

Figure 2. Activation of caspase 3/7 after 48-hr exposure to ellagic acid. Data points are expressed as the arithmetic mean ± S.E.M.

Based on these results, ellagic acid was found not to contribute to the pro-oxidative capabilities of the pomegranate extract and did not induce cell death through the formation of reactive oxygen species. Apparently, ellagic acid per se, not its auto-oxidation products, was the cytotoxic agent to the oral carcinoma HSC-2 cells through its induction of apoptosis.

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Student Researcher
Bella Wolf is a sophomore at Stern College for Women and is majoring in Biology. She hopes to continue on to medical school after college and become an ophthalmologist.
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Cancer Biology

Bilberry Extract: A Pro-oxidant Nutraceutical with Toxicity towards Glioma C6 Cancer Cells

by

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Positive health effects of the consumption of fruits, berries, and vegetables have been associated, in part, with their high content of polyphenols that provide antioxidant activities among other beneficial properties. Interestingly, at alkaline pH levels these same phytochemical polyphenols undergo autooxidation reactions to generate reactive oxygen species (ROS). Studies with extracts from cactus pear, apple, pomegranate, and *Gingko biloba*, as well as much research with green and black tea polyphenols have shown that the pro-oxidant activities of natural plant extracts may exert selective cytotoxicities towards cancer cells. Little is known of the anticancer properties of bilberry (*Vaccinium myrtillus*), a small shrub common in hilly regions of Europe, Asia, and North America, and has been used in traditional medicine since the Middle Ages. The polyphenol anthocyanosides constitute the biologically active fraction of this berry. Bilberry anthocyanosides absorb well via the oral route, resulting in elevated plasma levels, and have known vasoprotective activities. Although the antioxidant property of bilberry is known, there are no studies of its potential pro-oxidant nature. The study herein evaluated whether bilberry extract has pro-oxidant activity and whether this activity is sufficient enough to be cytotoxic to neuronal cancer cells.

Using the FOX assay, the pro-oxidant nature of bilberry extract was evaluated after a 4-hr incubation in cell culture medium. The principle of the FOX assay is based on the generation of hydrogen peroxide (H_2O_2) by a test agent involving the oxidation of Fe^{2+} to Fe^{3+}, which subsequently reacts with xylenol orange to yield a xylenol orange-Fe^{3+} complex that can be measured spectrophotometrically at 595 nm. Progressively increasing the concentration of bilberry extract from 5 to 300 μg/ml yielded concomitant increases in the amount of H_2O_2 in a pyruvate-free medium. To ascertain that H_2O_2 was the specific ROS accounting for the oxidation of Fe^{2+} to Fe^{3+}, the experiment also was performed in cell culture medium containing 110 mg/L of pyruvate, a scavenger of H_2O_2. Hydrogen peroxide decarboxylates pyruvate to acetate and liberates CO_2. In the presence of pyruvate, the detection of H_2O_2 was significantly lowered, indicating that H_2O_2 was the oxidant produced from the autooxidation of bilberry extract polyphenols (Figure 1).

To determine whether the level of generated H_2O_2 was significant enough to exert cytotoxicity, the antiproliferative effects of bilberry extract were evaluated using rat glioma C6 cells as the bioindicator cells and the neutral red (NR) assay as the cytotoxicity endpoint. The NR assay is based on the uptake and accumulation of the supravital dye, NR, by healthy, undamaged cells. Briefly, the procedure for the NR assay was as follows: Individual wells of a 96-well microtiter tissue culture plate were seeded with 2 x 104 cells in growth medium (DMEM + 10% fetal bovine serum (FBS)). After one day of incubation, the growth medium was removed and replaced with exposure medium (DMEM amended with 10% Serum Plus, 2% FBS, and without and with 110 mg/L pyruvate), amended with 5 to 300 μg/ml bilberry extract and incubated at 37° C for 24 hr. One complete row, i.e., 8 wells, was used for each concentration of extract. After a 24-hr exposure, cell viability was assessed. The medium was removed, NR-containing medium was added to each well and incubation was continued for 1 hr at 37°C. Cells were then rapidly washed and fixed with a solution of 0.5% formalin-1% $CaCl_2$ and the NR incorporated into the viable cells was released into the supernatant with a solution of 1% acetic acid-50% ethanol. Absorbance was recorded at 540 nm with a microtiter plate spectrophotometer.

The cytotoxicity of bilberry extract to C6 cells was greatly reduced, but was not completely abolished, in the presence of pyruvate (Figure 2). Apparently, autooxidation of bilberry extract polyphenols generated H_2O_2 at levels significant enough to evoke a cytotoxic effect. However, cytotoxicity was not

completely eliminated in the presence of pyruvate, thereby indicating that the overall antiproliferative effects of bilberry extract were due to a combination of the polyphenols *per se* and of H_2O_2.

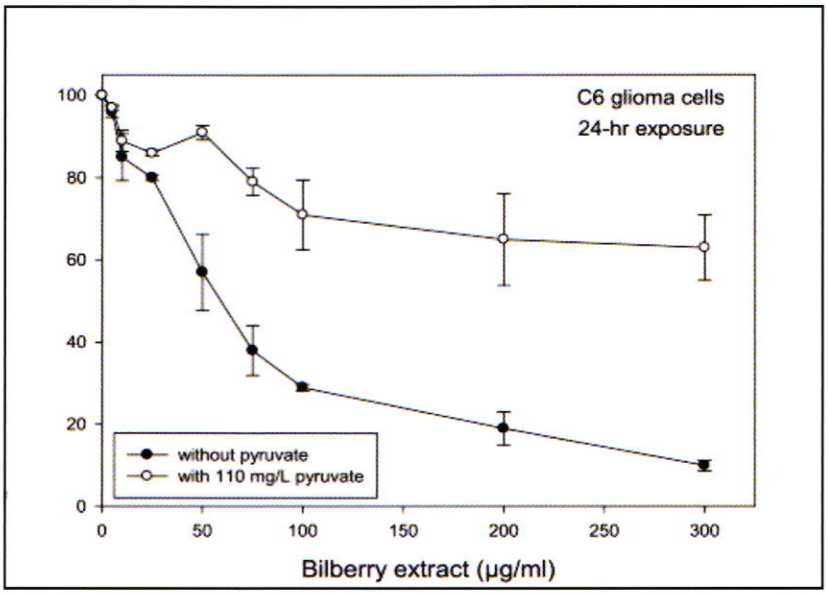

Figure 1. Generation of hydrogen peroxide in cell culture medium without and with pyruvate.

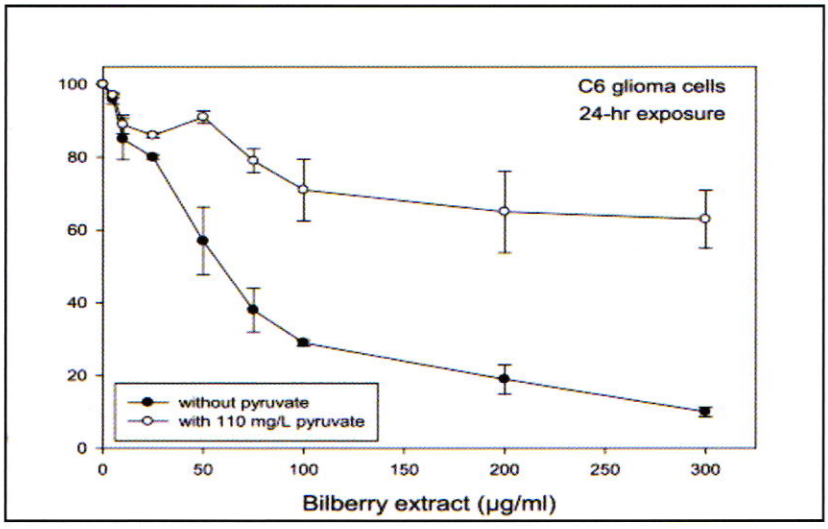

Figure 2. Comparative toxicity of bilberry extract to C6 cells in the absence and presence of pyruvate.

Student Researcher
Liorah Sabbah is a recent Stern College graduate with a degree in Psychology and Neuroscience concentration. Liorah grew up in Tahiti and bravely moved to New York after high school to pursue her college education at Stern College. She is now on her way to obtain a PhD in Neuropsychology. Liorah hopes to continue being involved in different types of neuroscience research for years to come and to one day run her own research laboratory.
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Cancer Biology

The Effects of Small Molecule Inhibitor LB-1 on the DNA Repair Pathways of the Migratory Subpopulations of Breast Cancer Cells

by

Eli Grunblatt and Sumanta Goswami

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A major problem in the world of modern oncology is the tendency of cancer patients to experience relapse of cancer following initial treatment with surgery, radiation or chemotherapy. Past research has shown that this tendency is linked to the resistance of invasive and migratory cancer cells to standard chemotherapeutic agents (1,2). It has been demonstrated that anti-apoptotic and DNA repair response genes are up-regulated while pro-apoptotic genes are down-regulated coordinately in the migratory subpopulation (1,2). This shows that invasive cancer cells are resistant to apoptosis inducing chemotherapeutic agents such as doxorubicin, etoposide, cisplatin, and tamoxifen (1,2). As such, a lucrative area in the modern cancer drug industry is the development of DNA repair inhibitors that can cause cancer cells to become more susceptible to the induction of apoptosis by standard chemotherapeutic agents and radiation.

Recently, a pharmacological agent known as LB-1 (4-(3-carboxy-7-oxa-bicyclo [2.2.1] heptane-2-carbonyl) piperazine-1-carboxylic acid tert-butyl ester) has been developed as an inhibitor of protein phosphatase 2A (PP2A), an enzyme that modulates pathways leading to cell cycle arrest and DNA repair (3). Previous research has shown that knocking out this enzyme in leukemia and cervical cancer cell lines using siRNA reduces cell DNA repair capabilities (4). When tested on several populations of brain cancer cells, LB-1 has been found to increase the susceptibility of the tumor cells to standard radiation and chemotherapy (3). Past work in our lab on MTLn3 (a rat breast cancer cell line), Met-1 (a mouse breast cancer cell line), and MDA 231 (a human breast cancer cell line) has demonstrated that LB-1 makes these populations more sensitive to treatment with doxorubicin.

The goal of this study was to ascertain if LB-1 played a direct role in the down-regulation of the DNA repair pathways of breast cancer cell populations. The primary technique used in this study was the single cell gel electrophoresis assay, also known as the comet assay. In this procedure, MTLn3 and MDA 231 cells were first treated with either LB-1, doxorubicin, or LB-1 plus doxorubicin and then irradiated to induce DNA damage. The cells were then allowed to recover from said damage. They were then layered in agarose gel on top of microscope slides and treated with an alkaline protein lysis and DNA denaturing solution. A gel electrophoresis was then run, after which the cells were stained with DAPI and imaged using epifluorescence microscopy in order to ascertain the degree of DNA damage in each individual cell.

The results of this study indicated that the cells that were treated with LB-1 and LB-1 plus doxorubicin exhibited a higher degree of residual DNA damage compared to untreated cells. This observation shows that LB-1 indeed plays a role in down-regulation of DNA repair and can be potentially used to increase the effectiveness of standard chemotherapy in eliminating migratory subpopulations of cancer cells in patients. Future research will focus on the effects of LB-1 on the metabolic pathways of breast cancer cells and the effects of other small molecule inhibitors on the DNA repair pathways of migratory cancer cell subpopulations.

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Student Researcher

Eli Grunblatt is currently a sophomore at Yeshiva College majoring in Chemistry and Biology and minoring in Psychology. In addition to studying all things science related, he also enjoys playing hockey and studying the linguistics of Indo-European languages.

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Cancer Pathology

Effect of Her-2 Levels on the Prognosis of Ductal Carcinoma In Situ (DCIS) as Indicated by Oncotype Recurrence Scores in Breast Cancer Patients

by

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Cancer is the result of an accumulation of mutations in genes that control cell growth and survival. Healthy cells proliferate to replace themselves with new cells as the older ones die. Cancer cells have a mutation that allows the cells to divide uncontrollably, resulting in the production of more mutant cells, which, in turn, forms a cancerous growth. Malignant tumors can spread to other parts of the body.

Breast cancer is a malignant tumor. The breast is made of lobules and ducts. Lobules are the milk producing glands while ducts are the means by which the milk is drained from the lobules to the nipple. Breast cancer usually begins in the lobules or ducts. Genetic and environmental factors play a role in the carcinogenesis process in breast cancer [1].

Ductal Carcinoma in Situ (DCIS) is the most common type of non-invasive (premalignant) breast cancer. It begins in the milk duct and does not spread to any surrounding tissue, hence it is non-invasive and not life threatening. It does, however, increase a patient's chances of developing invasive breast cancer in the future. According to the American Cancer Society, approximately 60,000 cases of DCIS are diagnosed each year, accounting for one in every five cases of breast cancer.
The most common type of invasive breast cancer is called Invasive Ductal Carcinoma (IDC); it is the cause of eighty percent of all breast cancer cases. It begins in the ducts and then spreads to the surrounding breast tissue.

Both DCIS and IDC are graded to determine the severity of the cancer (Grade I, II, III). The higher the grade, the more severe the cancer is and the higher the chance of recurrence. Often, DCIS and IDC are found in the same tumor.

The Her-2 gene (human epidermal growth factor receptor 2) plays a role in breast cancer development. Multiplication of this gene causes breast cells to grow and divide uncontrollably. If there are too many HER-2 receptors, the cells over-respond to growth factors, which in turn will amplify the cancer's growth. If a patient is tested positively for Her-2, she can be treated using Herceptin to block these receptors; this will decrease the cancer's growth rate. Herceptin is an antibody against the Her-2 receptor. If a patient is negative for HER-2 in both DCIS and IDC, there will be no need for Herceptin, and if the patient is positive for HER-2 in IDC, then there will be a response to Herceptin, regardless of whether DCIS is positive or negative. However, what will be the prognosis for a patient who is negative for Her-2 in IDC but positive for Her-2 in DCIS? Is it different from the prognosis of women who are negative for both IDC and DCIS?

Many of the women diagnosed with breast cancer have estrogen receptor (ER+) positive cancer. If a patient is ER+, it means that the cancer is fueled by the estrogen hormone; it can be treated using therapies that block or lower circulating estrogen levels in the body.

Oncotype DX is a test with both a prognostic and a predictive significance. It predicts the likelihood of breast cancer recurring in women who are ER+, and calculates the possible benefits of chemotherapy. To calculate the recurrence score, a panel of 21 genes is analyzed. The score ranges from 0 to 100.

The test was originally designed for women whose cancer is node-negative, meaning that the cancer has not spread to the lymph nodes. The test helps to decide if the patient would benefit from chemotherapy in addition to the anti-hormone treatment. Subsequently, the test has also been used for patients who are node positive.

Use of the Oncotype DX test is currently non-diagnostic for patients with DCIS only. Some of the patients who are ER positive, Her-2 negative in the invasive component of their cancer are also Her-2 positive in the DCIS component of the tumor. It is not known whether this finding bears any significance.

In the present study, we are attempting to correlate Her-2 levels in the DCIS component with the Oncotype DX score of the tumor. Data was collected from 186 patients. The cancer tissue was analyzed microscopically to determine the Her-2 level in the DCIS component. Their oncotype score was correlated to the degree of their DCIS Her-2 level. A conclusion has not yet been reached, as the research is still ongoing. Of the 186 patients so far, only 13 had high expression levels in the DCIS component, along with low levels in the invasive portion. The study will require a total of 60 such patients.

References

[1]*http://www.breastcancer.org/symptoms/types/dcis/*

Student Researcher

Tova Schiff is a junior at Stern College for Women, majoring in Biology. The research was conducted in the Department of Pathology at Shaare Zedek Medical Center in Jerusalem. Upon graduation, Tova hopes to pursue a career in the pharmaceutical industry.

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Cancer Biology

Metastasis and Invasion of CXCL12 Breast Cancer Cells

by

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Breast cancer is the second leading cause of cancer-related deaths in women. This high mortality rate associated with breast cancer stems from the development of metastatic disease. The metastasis cascade consists of a multi-step process that involves the spread of cancer cells from the primary tumor site to secondary organs and tissues through processes of invasion, intravasation, extravasation and survival/growth of cancer cells at new sites. Previous studies have shown that breast cancer malignancy can be enhanced through a paracrine loop interaction between breast cancer cells and tumor associated macrophages utilizing epidermal growth factor (EGF) and colony stimulating factor 1 (CSF-1). It was found that the EGF/CSF-1 paracrine loop between tumor cells and macrophages can be modified by different ligands secreted by breast cancer tumor cells. CXCL12 is a chemokine that has been found to stimulate invasion, and it has been shown that CXCL12 stimulates tumor cell invasion *in vitro*, as well as plays a key role in the metastatic behavior of these cells in vivo. Recent work in our lab has determined that increased expression of CXCL12 by MTLn3 rat mammary adenocarcinoma cells can recruit additional macrophages and increase tumor cell invasiveness. Our hypothesis is that the over-expression of chemokines by tumor cells can enhance invasiveness through stimulation of macrophages using the paracrine loop. The study will test this hypothesis by expressing different chemokines (CXCL12, CCL2, CCL4, CX3CL1, VEGFA and IL8), whose expression is correlated with poor prognosis, in MDA-MB 231 ATCC human breast cancer cells and further evaluating whether or not there is an effect on invasiveness and metastasis. We have generated stable transductants of MDA-MB-231 cells carrying the CXCL12 expression constructs using two expression vectors: pLEX and pQCXIP. Our results from the ELISA validated the overexpression of CXCL12 in these transductants. Future work will be done in order to determine if expression of CCL2, CCL4, VEGFA, CX3CL1 and IL8 in the 231 ATCC and MTLn3 cell lines also increases tumor associated macrophage density and *in vivo* invasiveness.

Acknowledgements

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Student Researcher

Jordana Schneider is a graduating senior at Stern College for Women double majoring in Biology and Psychology. She intends on pursuing a career in medicine where she can additionally perform research in the field of stem cell therapeutics. Jordana dreams to one day play a part in the discovery of cures for world-wide diseases.

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Cardiology

Pericardial Inotropic Drug Delivery

by

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Cardiac surgical patients with myocardial dysfunction are at risk for exacerbated cardiomyopathies, especially following the use of cardiopulmonary bypass (CPB). Inotropic drugs are used to increase the force of myocardial contraction and separate heart failure patients from CPB. However, systemic side effects such as peripheral vasodilation and hypotension limit their dose and utility, and often require infusion of other medications to ameliorate these peripheral effects. Local pericardial delivery may allow inotropes to work on the heart without peripheral side effects, allowing for higher drug concentrations within the myocardium and enhanced effect. The dose response to dobutamine was compared with intravenous (IV) infusion and pericardial (PC) controlled-release.

A Millar pressure-volume conductance catheter was used in rats to assess contractility. Animals were anesthetized, ventilated, and cannulae were placed in the femoral artery and right internal jugular vein. A Millar conductance catheter was advanced retrograde from the carotid artery into the left ventricle. Dobutamine was given by IV infusion or released from a PC alginate disk over a range of rates (0 to 4 mcg/kg/min). The contractility was assessed as the maximal rate of change of pressure in the left ventricle (dP/dt-max).

PC dobutamine maximally raised dP/dt-max by 83% while IV infusion raised it 24%. ED50 for PC and IV administration was approximately 0.8 and 1.4 mcg/kg/min, respectively. ED95 for PC and IV administration was 1.5 and 2.5 mcg/kg/min, respectively. At equal rates of administration, systemic vascular resistance decreased by 41% for IV infusion and only 20% for PC release.

The same drug given by different means shows not only differential potency and peripheral side effect, but also a dramatically different biologic effect. Pericardial application of dobutamine is more efficacious than intravenous infusion. These data suggest that targeted PC application of inotropes may be a valuable approach to treating cardiac surgical patients with profound cardiomyopathies.

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Student Researcher

Sarah Lazaros is a senior at Stern College majoring in Women's Studies. A radical feminist, Sarah is applying to medical school this summer with hopes to pursue an MD/MPH. She believes passionately in preventive and primary care medicine. Her biggest pet peeves are wastefulness and people who do not recycle.

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Endocrinology

Normocalcemic Primary Hyperparathyroidism: Variability of PTH in Normocalcemic Patients and Possible Etiologies

by

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The main function of parathyroid hormone (PTH) is to maintain the appropriate calcium and phosphorous levels in the blood. Elevated parathyroid levels are usually associated with high blood calcium levels, a condition called Primary Hyperparathyroidism (PHPT). This is caused by a benign solitary adenoma or, less commonly, by hyperplasia of the parathyroid glands. Low levels of Vitamin D can also cause high PTH levels. Although classical PHPT is manifested by hypercalcemia, an increase in blood calcium levels, recently it has been found that people with normal calcium levels can show elevated PTH levels. This has been classified as normocalcemic hyperparathyroidism (HPT), a condition in which patients maintain normal calcium levels but exhibit elevated PTH levels. The significance of elevated PTH levels in the absence of hypercalcemia is not understood. The present observational study was done in order to characterize the significance of normocalcemic hyperparathyroidism as the condition may have implications for bone disease, kidney function, and cardiovascular disease.

Original data (medical records) of 24 women from 1983 until 2011 were reviewed. Patients were studied for a mean of 9.8 years (range 1-28 years). PTH and calcium levels were tracked together with Vitamin D levels. Ionized calcium levels were measured in some of the subjects. Twenty-four urine calcium and creatinine measurements were also collected from patients. Since PTH is a known cause of low bone density and all subjects displayed low bone density, all subjects had their PTH measured even though they exhibited normal calcium levels.

We discovered that only 2/24 of the patients displayed high ionized calcium levels, which is a defining feature of hypercalcemic hyperparathyroidism. Furthermore, 16/24 of the patients displayed fluctuating levels of PTH (an example of which is shown for one patient in Figure 1). Fluctuating levels of PTH are defined as PTH levels which elevate, return to normal, and then elevate again at seemingly random time intervals.

These findings are significant because they allow for a better characterization of normocalcemic hyperparathyroidism and shed light onto whether it is a disease unto itself or a precursor to hypercalcemic hyperparathyroidism. In a majority of patients with normocalcemic hyperparathyroidism, progression to hypercalcemia is not observed. As such, conservative management is recommended and surgical correction may not be needed.

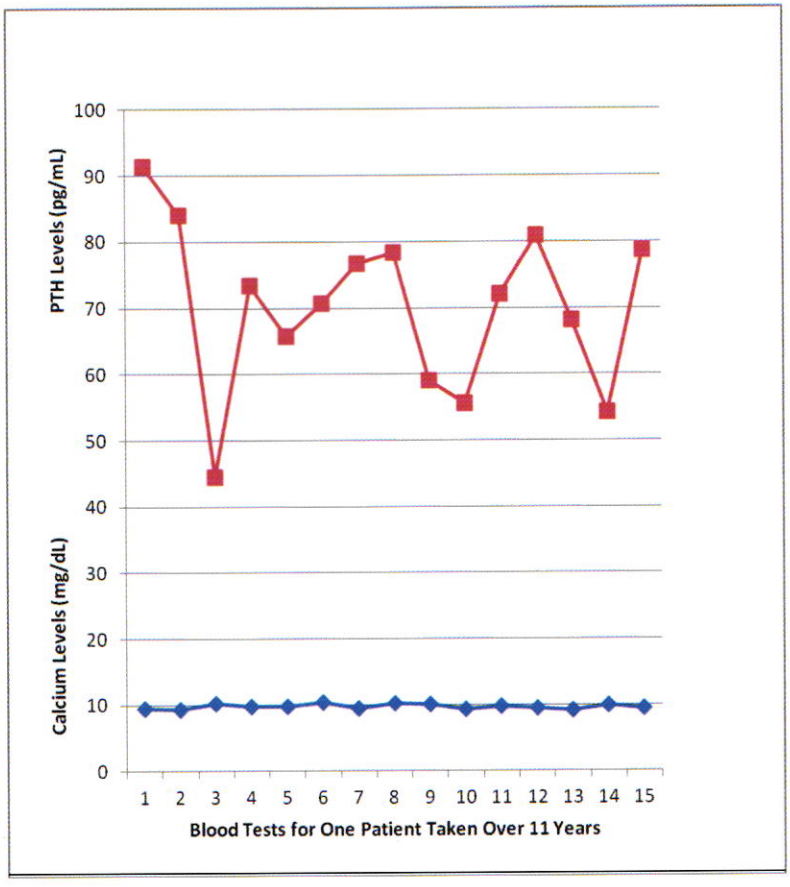

Figure 1. Blood test results for one patient taken over 15 different patient visits show fluctuating PTH levels but normal calcium levels over time. Calcium Levels (in blue) remain within normal range of 8.5 – 10.5mg/dL while PTH levels (in red) fluctuate between measurements above and within the normal range of 10-65pg/mL.

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Student Researcher
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Endocrinology

Correlation Between Markers Involved in Increased Risk for Developing Gestational Diabetes Among Chinese Women

by

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Gestational Diabetes Mellitus (GDM) is a pathological condition affecting approximately 3.2-5% of pregnancies with about 135,000 cases occurring annually in the United States. GDM occurs when women without previously diagnosed diabetes exhibit high glucose levels and poor glucose tolerance during pregnancy, especially during the third trimester. Women who develop GDM are unable to compensate for the increased insulin resistance state characteristic of pregnancy due to their diminished beta cell reserve. Infants born to mothers suffering from gestational diabetes may develop jaundice, exhibit abnormal levels of blood sugar, and become large for their gestational age, which can complicate delivery.

This study aimed to compare biochemical markers that influence insulin resistance in Chinese-American and Caucasian women who develop GDM. Chinese women, when compared to Caucasians of a similar body mass index, have a significantly increased risk of developing GDM. The frequency of gestational diabetes among Chinese women is 5.6%-6.22%, while it afflicts only 2.5%-3.8% of Caucasian women. Additionally, the Chinese population exhibits higher insulin levels than the Caucasian population. The discrepancy may be due to genetic variance and mutations in the Chinese population that can be identified by biochemical markers.

189 Chinese American women at 24-28 weeks gestation were examined for the following markers: insulin, T-APN & HMW-APN, CRP, TNF-α , IL-6 and MCP-1 at the time of their 50-gm glucose challenge test. Pearson correlation coefficients for glucose (1HGCT), Hemoglobin A_{1C} (A1C), and BMI were calculated against the markers described above. HgA_{1C} (A1C) is a form of hemoglobin that serves as an identifier of average plasma glucose concentrations because the fraction of glycosylated hemoglobin positively correlates with glucose levels.

Patient blood samples were analyzed to measure levels of these biochemical markers. Most significantly, adiponectin, a protein hormone secreted by adipose tissue which modulates glucose regulation and fatty acid catabolism, was found to be present in lower levels in patients with gestational diabetes. Both T-APN & HMW-APN correlate inversely with 1HGCT, insulin, and BMI in pregnant Chinese American women. In addition, T-APN inversely correlates with A1C in these women. In contrast to the Caucasian GDM studies, no significant correlations were observed between the markers of glucose intolerance (1HGCT, A1C, insulin, or BMI) and inflammatory markers (TNF-a, IL-6 or MCP-1).

The ability to identify markers indicative of the development of gestational diabetes could potentially improve pregnancy and neonatal health by leading to earlier treatment and better modulation of gestational diabetes within the Chinese community.

Student Researchers

Samantha Selesny is a junior majoring in Biochemistry and aspires to pursue a career in medicine. She is president of the YU Academic Honesty Committee and is a member of the volleyball team. In her free time, Samantha also enjoys to ski and snowboard.
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Amanda Elmakiyes is a senior majoring in Biochemistry. She is involved in the Global Health Club and has worked to coordinate many of their events. She would like to pursue a career in medicine, specializing in pediatrics.
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Immunology

Regulatory Mechanism of WASp: A Key Regulator of Actin Cytoskeleton Machinery

by

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The actin cytoskeleton of leukocytes plays an important role in the immune response by controlling the shape of the cell, thus facilitating cell movement, invasion through tissues, and adhesion with a target cell. The objective of the lab research is to focus on actin-cytoskeleton-regulating proteins in lymphocytes. Aberrant regulation of cytoskeletal proteins can lead to hyper-reactive T-cells which can result in auto-immune disease. Furthermore, a lack of these proteins can lead to primary immunodeficiencies such as the Wiskott-Aldrich syndrome (WAS) and X-linked thrombocytopenia (XLT). These diseases are characterized by recurrent infections, and hematopoietic malignancies. Genetic deficiency of the Wiskott-Aldrich Syndrome Protein (WASp) was identified as the causative defect in WAS and XLT.

Using the gene silencing approach together with biochemical analysis, we examined the influence of WASp on T-cell signaling. Using these same techniques we were able to silence the WASp Interacting Protein (WIP), a chaperone protein of WASp, in order to examine its role in WASp regulation in future experiments. The characterization of the regulation of cytoskeletal proteins will provide us with better understanding of the immune response, help identify causes of immune diseases, and allow us to offer therapeutic approaches to treat these diseases.

Student Researcher

Shimon is currently a senior in YC majoring in Biology. He plans on pursuing a career in medicine, and is currently studying for a rabbinic degree as well. He has a keen interest in Jewish medical ethics and enjoys researching and lecturing on various topics within the field. Shimon enjoys debating, swimming, relaxing with friends, traveling the world, and taking long walks on the beach.

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Immunology

Engineering Soluble T Cell Receptors as Therapeutic Molecules

by

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HIV infected cells present viral peptides in the form of MHC proteins on their external membrane surfaces. Cytotoxic T cells of the immune system express T-Cell Receptors (TCRs) that recognize MHC proteins, and hence, effectively target and kill infected cells. Our lab seeks to understand the structural basis upon which TCRs recognize the MHC+ cognate viral peptide of HIV and to develop, based on the TCR - MHC+ cognate interactions, novel therapies to kill HIV-infected cells such as using soluble TCRs. The benefits of using soluble TCRs to recognize and eliminate HIV cells are that TCRS are highly specific and sensitive and detect infection early on in the replication cycle. These advantages allow for the specific targeting and elimination of infected cells before they propagate viral progeny. By conjugating the TCRs to a toxin, we can deliver toxins specifically to HIV-infected cells to eliminate them. Using an engineered TCR, we have been able to successfully produce soluble TCRs in mammalian cells and subsequently isolate purified protein from the cell supernatant through affinity purification. In an attempt to increase soluble TCR production, we have cloned the TCR genes on a single plasmid with a "self-cleaving" 2A peptide to allow for equimolar expression of the two genes enabling for efficient production of the TCR heterodimer. To further increase protein production, we have incorporated this construct into a lentiviral expression vector to generate stably transfected cells producing high concentrations of the TCR. We hope to use these laboratory advancements to further our progress towards an effective therapeutic for HIV.

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Student Researcher

Ike Levine is a senior at YU majoring in Chemistry. Ike has served as a research assistant in the research laboratory of Dr. Harris Goldstein of Albert Einstein College of Medicine for the past two summers and during the academic semester works as a teacher's assistant for Professor Barrios-Landeros of Yeshiva College. For fun, Ike enjoys playing the piano and competing in basketball tournaments. After graduation, Ike aspires to become a physician.

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Microbiology

Investigation on Replicative Life Span of Clinical and Environmental *C. neoformans* Strains

by

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Replicating eukaryotic cells, such as *Cryptococcus neoformans* undergo asymmetric cell divisions in a process known as replicative aging. The replicative life span (RLS) of *C. neoformans* strains is not known. Hence, the objective of this study was to obtain baseline data on RLS of both clinical and environmental *C. neoformans* strains. Senescent "mother" cells can be distinguished from virgin "daughter" cells and micro-manipulated with a dissection needle on YPD agar to determine their RLS. Clinical strains were incubated at 37°C and environmental strains at 30°C between dissections. Median RLS of clinical strains ranged from 12 to 67 generations and limited analysis did not suggest a significant difference in life span between 6 serotype A strains (Median RLS of 31.25 generations) [H99, I47, I55, ISG12, I58, I65], and 5 serotype D strains (Median RLS of 41.8 generations) [RC-2, JEC21, I114, J22, J9]. Median RLS (49.5) of 2 environmental strains [B10, E6] did not suggest a significant difference in life span between environmental and clinical isolates, however this needs to be confirmed with more strains. Analysis of RLS demonstrates that the majority of yeast cells from clinical strains divided every 2 hours initially, and significantly slowed doubling time in the last third of lifespan, whereas environmental strains divided every 1.25 hours initially and also slowed significantly in the last third of lifespan. Next, the effect of temperature on RLS was investigated. RLS analysis at 30°C versus 37°C differed moderately, but inconsistently for H99 (33.5+/-7.73 versus 27.0+/-9.71). We also determined that there is variability in cell body size and volume between environmental and clinical strains, specifically, the cells in the clinical strains appeared significantly larger than those in the environmental strains.

In summary, RLS of several *C. neoformans* strains was successfully determined and found to vary among strains and was in the range of the life span described in the *S. cerevisiae* strain. Size appears to vary between clinical and environmental strains. Though these findings must be further substantiated by analysis of bigger collections, they support the concept that RLS of *C. neoformans* is variable and that some differences exist between clinical isolates and environmental strains.

Student Researcher

Marc Fenster is a senior at Yeshiva College. He is a Biology major and plans to apply to medical school this summer.

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Microbiology

Effects of TiO_2 and ZnO Nanoparticles on Healthy and Infected Macrophages with *Leishmania tropica* and *Staphylococcus aureus* In Vitro

by

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Leishmaniasis, a potentially lethal disease that affects over 12 million people, is caused by the parasite *Leishmania*. The parasite accrues in the vacuoles of cells and propagates from amastigote to promastigote, killing the host cell. Titanium dioxide (TiO_2) and zinc oxide (ZnO) nanoparticles generate free radicals with varying potency, as measured through D&C Red No. 28 dye degradation and DNA gel electrophoresis experiments.

In the current study, these nanoparticles were added in various concentrations to *Leishmania*-infected J774A.1 macrophages, which have cell membranes with increased porosity due to the parasitic infection. Results showed that after 24 hours with a 100% parasite infection rate, only 40% of the macrophages were alive and multiplied in the presence of TiO_2 rutile at 0.2 mg/mL, therefore concluding that the infected cells were killed at a higher rate. To further verify the suitability of rutile as a cure for leishmaniasis, the infectivity index was taken. The index showed that though rutile treatment increased the percentage of macrophages infected with *Leishmania*, it also resulted in the lowest number of parasites per macrophage when compared to that of gold and ZnO nanoparticles. This implies that rutile is very effective and efficient at killing *Leishmania*.

In a separate experiment, macrophages were exposed to *Staphylococcus aureus* bacteria in the presence of nanoparticles to examine how nanoparticles affected macrophage immune function. Results showed that ZnO does not significantly hinder immune function, but TiO_2 decreases immune function by approximately 30%. However, the benefit of a new drug utilizing TiO_2 rutile nanoparticles against *Leishmania* may outweigh the risk of a disadvantaged immune system during treatment. This cure is effective and inexpensive, and is much needed in poverty-stricken communities where leishmaniasis is most prevalent.

Student Researcher

Chana Stern is currently a sophomore at Stern College for Women majoring in Biology. Chana hopes to actualize her long-time dream of becoming a physician after her undergraduate studies. For fun, she enjoys taking long walks around the city and spending time with friends.

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Microbiology

Combating Fungal Infections with Nanoparticle Encapsulated Amphotericin B

by

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Amphotericin B (AmB) is a commonly used antifungal drug which has severe side effects that can lead to serious complications. In the past, the Nosanchuk lab has successfully used silane-based nanoparticles as a therapeutic delivery mechanism. The nanoparticle's size theoretically allows it to slip through the fungi's extracellular biofilm and directly target the microbe, while concomitantly limiting drug toxicity.

Nanoparticle encapsulated AmB (np-AmB) preparations were prepared according to developed protocols and the release kinetics of the drug were studied. Different concentrations of both solubilized AmB (s-AmB) and np-AmB were delivered to standard populations of *Candida albicans (CA)*. Metabolic assays with XTT salt were taken at specified intervals. In a parallel experiment, each concentration of the AmB was applied to an established *CA* biofilm, and the yeast cells were then collected and plated on YPD agar to compare growth rates. The results describe a steady release of AmB from the nanoparticles and show the np-AmB to be as efficient as the solubilized AmB in the inhibition of *CA* growth. Finally, the np-AmB was delivered to twelve strains of *Candida*, and the np-AmB exhibited similar or increased efficacy compared to the s-AmB.

The study suggests a novel method of delivery of AmB. For treatment of focal fungal disease, such as in an infected intravenous catheter or a cutaneous infection, np-AmB, which slowly and steadily releases the drug, would likely have less toxicity than s-AmB. In addition, the study demonstrates encapsulation of AmB by our methods does not inhibit the efficiency of the drug. Hence, the np-AmB is a promising new formulation of a potent antifungal that can be adapted for diverse clinical purposes.

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Student Researcher

Daniel Rosen is a graduating senior at Yeshiva University majoring in Biology. Daniel looks forward to putting his Torah values and love of the sciences into practice as he journeys on to medical school next year. In his spare time, Daniel enjoys spending time with friends, learning new things, and volunteering as an EMT and NCSY advisor.

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Molecular Genetics

Genetic Analysis of Homomeric and Heteromeric Interactions of HIV-1 Integrase with the Host Factor INI1/hSNF5

by

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HIV-1 Integrase (IN) is a virally encoded enzyme that catalyzes the integration of viral DNA into host genome. IN exhibits both homomeric and heteromeric protein-protein interactions. INI1/hSNF5 is a host protein that directly binds to HIV-1 IN. It is a core component of the ATP-dependent chromatin-remodeling complex, SWI/SNF, and is also a tumor suppressor. INI1 is required for HIV-1 particle production, is encapsidated into HIV-1 virions and is required for infection of particles. Previously, a yeast reverse two-hybrid system was used to isolate INI1-interaction-defective (IID)-IN mutants. These IID-IN mutants, such as D202G, were severely impaired for replication.

A yeast two-hybrid system was used to characterize homomeric interactions of D202G mutant and to isolate compensatory mutations in INI1 that restores the interaction with D202G. To determine the homomeric interactions, plasmids encoding GAL4-Activation Domain (GAL4-AD) fused to IN (WT or D202G) were co-transformed with plasmids encoding LexA DNA binding domain (LexA-DB), also fused to IN (D202G or WT), into yeast. The interaction between IN-IN, IN-D202G and D202G-D202G were assessed based on their ability to induce the *LacZ* reporter gene expression using an X-Gal assay. We found that D202G IN retained homomeric interactions indicating that it is specifically defective for interaction with INI1.

To screen for mutants of INI1 that acquired the ability to bind to D202G, a random INI1 point mutation library (GAL4-AD-IN*) was co-transformed into yeast along with LexADB-D202G. Initial screening of 30,000-40,000 yeast transformants has yielded several blue colonies. We are in the process of isolating and sequencing the plasmids from these colonies to determine the nature of mutations that may have conferred INI1 ability to bind to D202G. Characterization of these compensatory mutations is likely to yield valuable structural information and may lead to rational drug design to combat HIV-1.

Acknowledgements

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Student Researcher

Menachem Spira is a fourth-year senior at Yeshiva College Majoring in Biology with a minor in Chemistry. He is particularly fascinated in laboratory research with an interest in the biochemistry of cellular immune responses. Upon graduation, Menachem plans to pursue an MD/PhD. In his limited free time, Menachem enjoys a good book and flash-freezing fruits in liquid nitrogen.

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Molecular Genetics

Understanding the Role of Intronic Cis-acting Elements in the Splicing of MacroH2A1 Variants

by

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The histone variant macroH2A replaces the canonical histone H2A in nucleosomes in specific regions of the genome in order to regulate gene expression. Two splice variants of macroH2A1, macroH2A1.1 and macroH2A1.2, are encoded by mutually exclusive splicing of two alternative exons. Most normal human cells express similar levels of macroH2A1.1 and macroH2A1.2.; however, work from our lab has shown that alternative splicing of macroH2A1 pre-mRNA, leading to a decrease in macroH2A1.1 expression, occurs in a variety of cancers. Additionally, ectopic expression of macroH2A1.1 represses cancer cell growth and induces senescence in a splice variant-specific manner. Therefore, it is important to determine the mechanism that regulates macroH2A1 splicing and determine how this mechanism is modified in cancer cells. In order to identify the cis-acting sequences that regulate macroH2A1 splicing, we designed a macroH2A1 minigene, which includes three introns of 600 base pairs each flanking the alternative exons. In A549 lung fibroblast cells, which only express macroH2A1.2, the macroH2A1 minigene only expresses the macroH2A1.2 spliced transcript; however, in MG-63 osteosarcoma cells, which normally express both macroH2A1.1 and macroH2A1.2, the minigene still only expresses macroH2A1.2. This suggests that the macroH2A1 minigene is missing critical cis-acting sequences that are necessary to accurately splice macroH2A1.1. Interestingly, several highly conserved elements exist in the introns flanking the alternative exons of this gene. By applying our mingene splicing assay we are systematically analyzing the contribution of these ultra-conserved regions to the regulation of macroH2A1 splicing.

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Student Researcher

Elisa Karp is a third year student at Stern College majoring in Biochemistry and Mathematics. Elisa hopes to pursue an MD, specializing in pediatric medicine, while continuing her scientific research. In her free time, she enjoys playing volleyball and solving crossword puzzles.

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Neurobiology

Stress Modulates Mitochondrial Gene Expression in the Rat Hippocampus

by

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Our recent research has shown that both acute and chronic stress cause changes in the expression of mitochondrial genes in the hippocampus, a brain region vital to memory formation and some types of cognition. Acute stress appears to reduce the expression of several genes on the mitochondrial chromosome, whereas chronic stress produces an increase in one of the same genes.

A large body of research has linked mitochondrial function to human diseases including cancer, Parkinson's disease, and depression. However, only a small number of studies have sought to examine how the genes on the mitochondrial chromosome, which is separate from the chromosomes in the nucleus, are regulated by environmental conditions in living animals. Mitochondria are unique cellular organelles since they are the only organelle which retains its own genome in animals. The genome is composed of 13 protein-coding genes, 22 transfer RNA genes, and two ribosomal RNA genes. Our research looked at the protein-coding genes for the NADH dehydrogenase complex I constituents ND-1, ND-3 and ND-6; as well as the expression of the complex V ATP-synthase subunit ATP-6. Both the NADH dehydrogenase complex I and ATP-synthase are essential for production of ATP.

Mitochondria are also responsible for the production and control of reactive oxygen species and programmed cell death. Their ability to produce cell death can result from damage due to overactivation or toxic insult. They are particularly important in the brain, as the brain requires 10 times more energy than other tissues. As such, disorders which effect mitochondrial function often present with neurologic symptoms.

Stressful circumstances increase energetic demands on the brain. Studies in recent years have shown stress may cause structural and functional changes in highly active brain regions such as the hippocampus. Acute stress is known to produce a number of rapid effects which are often opposed to those observed after chronic stress. Further, we, and others have shown that stress hormone receptors enter hippocampal mitochondria and alter their function. To determine if stress was acting directly on mitochondrial genes, we subjected 3 month old rats to either a 30 minute acute stress, or a longer stress which was repeated daily for 3 weeks. We then examined how the stress changed the messenger RNA expressed by the mitochondria resident in the hippocampus. We found that after an acute stress, expression of four mitochondrial genes, ND-1, ND-3, ND-6 and ATP-6, was decreased more than 50% (Figure 1), suggesting a need to suppress mitochondrial activity after it was stimulated by stressful circumstances. Chronic stress showed an increase in the expression of one of these genes, ND-6, which may represent an adaptation to the higher energetic demands placed on the hippocampus in a chronically stressful environment. Our results provide evidence that mitochondria are capable of local energetic plasticity in response to stressful environmental circumstances and provide a new window on our understanding of stress's impact on brain function.

As mitochondrial function has been implicated in a number of diseases, including certain neurodegenerative diseases like Alzheimer's, which preferentially attack regions like the hippocampus, it would be interesting in future studies to examine the impact of stress in the context of aging on mitochondrial gene expression and function. Much work has established that mitochondrial dysfunction is present in the aging brain, but to date, none have examined how changes in mitochondrial gene expression might contribute, or how stress might worsen that contribution. Therefore our work has important implications for our future understanding of a variety of brain diseases, particularly those associated with aging and stress.

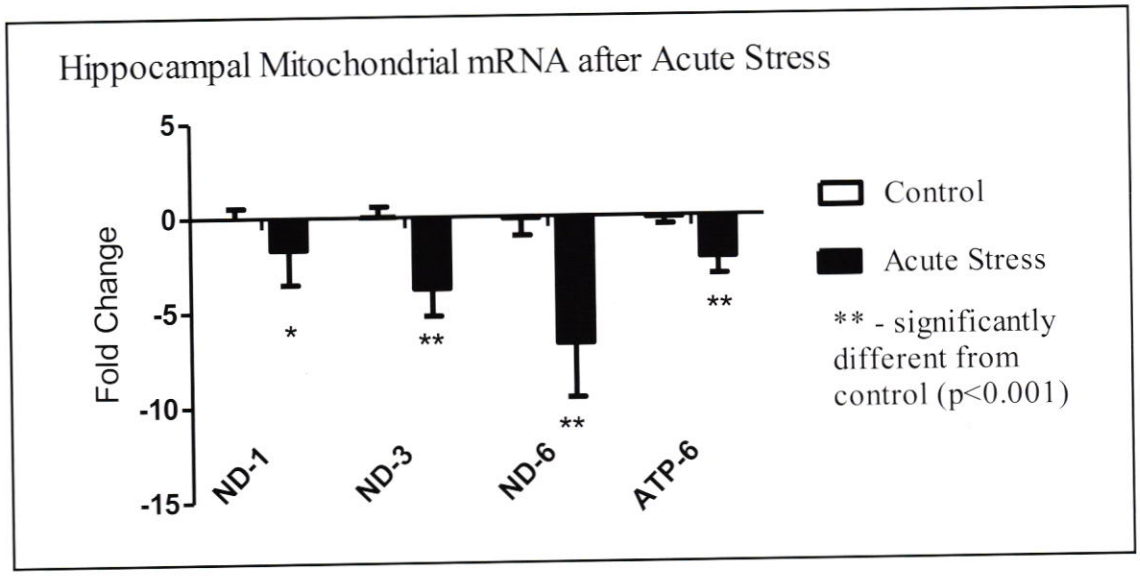

Figure 1. Graph depicts the downregulation of ND-1, ND-3, ND-6, and ATP-6 in rat hippocampal mitochondrial mRNA after acute restraint stress. There was a significant main effect of Stress, ($F=74.12$, $p<0.0001$).

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Student Researcher
Ma'ayan Hachen is a senior at Stern College for Women majoring in Neurobiology. She has been conducting neuroendocrinology research at Rockefeller University for the past two years and hopes to pursue a PhD in the field. She has tremendously enjoyed her time at Stern College and wishes to express her gratitude to the Henry Kressel Research Scholarship Program for giving her the support to continue her research.
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Neurodegenerative Diseases

Differentiating SH-SY5Y Neuroblastoma into Neurons using Retinoic Acid

by

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Development of an accessible source of human neurons is desirable for many types of studies, one of which includes neurodegenerative diseases. SH-SY5Y neuroblastoma cells are a line of transformed neuronal precursor cells that have been used in many studies. In our work, we tested several methods to induce these proliferating cancer cells into neuron-like cells. Molecules we used included retinoic acid (RA), cytosine arabinoside (ara-C), Rho kinase inhibitor (Rock), and nerve growth factor (NGF). Twenty four-well plates were seeded with 5,000-100,000 cells and then treated either with RA alone, RA accompanied by ara-C, or ara-C with NGF and Rock. We found that treatment of 15,000 cells with RA alone for 7 days effectively differentiated the neuroblastoma cells. Many of the resulting differentiated cells displayed neuronal morphology including round cell bodies and axon-like processes. In addition, immunostaining for specific neuronal markers confirmed the neuronal phenotype. Our results show that treatment with RA can be used as an inexpensive and efficient method to differentiate neurons from neuroblastoma cells, a process that can significantly aid further biomedical research.

Acknowledgements

We would like to thank Ronit, Igor, and Prof. Ron Goldstein for welcoming us into his lab. We would also like to thank Dr. Anatoly Frenkel and Dr. Chaim Sukenik for making the Bar-Ilan Program an amazing experience.

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Student Researchers

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Erica Hasten is a Biology with Concentration in Molecular/Cellular Biology major at Stern College. She especially enjoys talking about DNA replication and bragging to all of her friends that she is taking one of the longest-named majors. Not only has she dissected chicken eggs with Gigi and Igor in Prof. Ron Goldstein's lab in Bar Ilan University, but she has played with Katushka plasmids as well. In her spare time, Erica is an active member of Stern's leading cult: The Soccer Team. She also can be found in The Observer's secret hideout laying out the school newspaper. Erica hopes to continue conducting research and earn a PhD.
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Neuroimmunology

Modulation of the Plasminogen Activator (PA) System as a Potential Therapeutic Target in MG: Involvement of TGF-β

by

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Myasthenia gravis (MG) is an autoimmune disease characterized by a fluctuating muscle weakness caused by antibodies to the nicotinic acetylcholine receptor (nAChR) at the post-synaptic site of the neuromuscular junction. The AChR antibodies reduce the number of the available AChRs and cause a defect in neuromuscular transmission. The animal model for MG, experimental autoimmune MG (EAMG), is widely used for studying numerous aspects of the human disease and for evaluating potential treatments. In our lab we used the EAMG model to assess the potential involvement of the plasminogen activator (PA) system in the development of EAMG.

Plasminogen activators are extracellular proteases that modulate cell-cell and cell-matrix interactions. Components of the PA system, namely tissue PA (tPA) and urokinase PA (uPA), are elevated in inflammatory areas and are involved in inflammatory neurological disorders. In an ongoing study in the lab, the involvement of the PA system in EAMG was evaluated by using mice lacking tPA (tPA ko). It has been found that the tPA ko mice developed a more severe clinical disease than the wild type (wt) mice. In addition, the tPA ko mice had a higher titer of anti-AChR antibodies, as well as a higher expression of the B-cell markers: $CD19^+$ and $CD45R^+$. In contrast, specific T- cell reactivity towards the T-AChR, was markedly reduced in the tPA ko animals. In an attempt to solve the paradoxical role of tPA seen in the development of EAMG, the relative number of T-regulatory cells (Tregs) which are important in maintaining self tolerance was determined. A reduction in Tregs in EAMG tPA ko mice as compared to wt mice was found. While the reduction in Tregs may explain the more severe disease seen in the tPA ko animals, the reason for this reduction of Tregs remains unknown.

In the present study we evaluated gene expression of the anti-inflammatory cytokine, TGF-β in tPA ko mice compared to wt mice. tPA is known to participate in the maturation of TGF-β, and TGF-β is important for the generation and development of Tregs. To evaluate gene expression of TGF-β, RNA was extracted from muscle and lymph node from EAMG induced tPA ko and wt mice. RNA was extracted using the 5-Prime Perfectpure RNA kit (GmbH, Hamburg) according to the manufacturer's protocol. cDNA was synthesized by reverse transcription and further PCR amplified on an ABI 7900HT Fast Real-time PCR system using reagents and protocols provided by Applied Biosystems (Foster City, CA). The results of real time PCR for TGF-β reveal a reduction in gene expression in the tPA ko mice in both lymph node and muscle compared to the wt (Figure 1).

The evident correlation between a deficient PA system and the reduction in TGF-β gene expression may explain the reduction in Tregs in tPA ko mice and the more severe disease seen in the ko mice. Further investigation into the molecular mechanisms underlying the severe EAMG seen in PA system deficient mice may facilitate our understanding of EAMG development. This knowledge may help develop potential treatment for MG by modulation of the PA system.

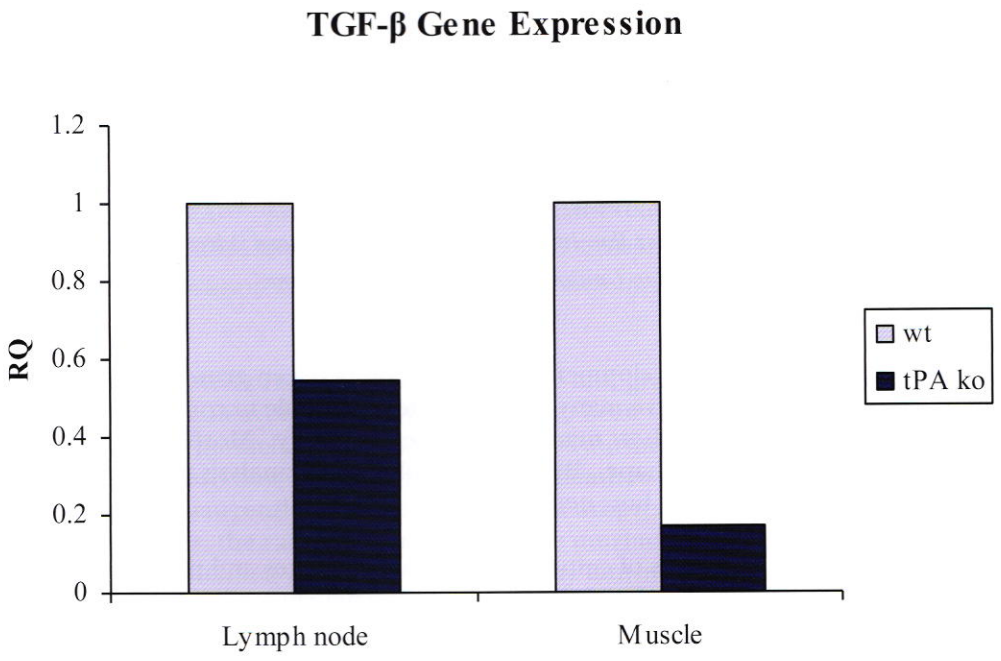

Figure 1. Relative quantification of TGF-β gene expression in EAMG tPA ko mice compared to wt mice in lymph node and muscle shows a reduction in the ko animals.

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Student Researcher
Lisa Cohen is a junior at Stern College majoring in Biology. She plans to pursue a career in the field of dentistry, with a specialty in fixed, removable, and implant prosthodontics. Lisa is currently a Biology TA and volunteers for the organizations Helping Hands and United Cerebral Palsy. She enjoys playing basketball in her free time and has played competitively on a team for many years.
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Neurobiology

Morphometric Study of Neurite Growth

by

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Neurites are "Dynamic"- during development they switch off between growing and retracting. The neuron must balance the need to have many, long neurites to be able to communicate with more, farther cells, and the need for few, short neurites to conserve energy. Morphometrics is the quantitative study of form such as size and shape. By using morphometric analysis to measure the lengths of neurites, it is possible to learn about how neurites grow.

We grew leech neurons on two types of culture plates - regular plates and plates with lines added onto them lithographically. We measured the lengths of the neurites using Neuron J, an Image J plugin created by Eric Meijering which traces neurites and measures their lengths. Using the measurements, we averaged the lengths of the neurites and the number of neurites for each day and made graphs of the data. We compared the neurite lengths and numbers for cells at different days of their growth after plating, and for each day we compared the lengths of neurons grown on the two types of culture plates. We also made graphs that differentiated between cells that contacted other cells and cells that stood alone.

Our results indicated that, for all types of plates, the sum of the neurite lengths for each cell and the number of neurites would increase for the first few days of development, but would then hit a peak and begin to decrease. However, the cells on plates with patterns had shorter neurites than the cells on the regular plates. Based on this data, we believe that the neurites grow until their neurites reach other cells, at which point they decrease the lengths of unattached neurites to conserve energy. The cells on the plates with patterns had shorter neurites because contact with the patterns was similar to contact with cells, so the cells began to diminish the lengths of their neurites earlier. This hypothesis is supported by our graphs comparing the cells with and without contact, from which it is evident that the cells without contact had longer and a greater number of neurites. This is likely because the neurites were still growing and searching for other cells with which to make contact.

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Student Researcher

Davida Kollmar is a junior at Stern majoring in Physics. She is a board member of both the physics and the chemistry club. Davida conducted this research as part of the inaugural Yeshiva University-Bar Ilan Summer Science Research Internship program.

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Neurobiology

Neuroprotective Actions of Taurine and Granulocyte Colony Stimulating Factor

by

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Recent studies have indicated protective roles for taurine and granulocyte colony stimulating factor (GCSF) against excitotoxic neuronal death. GCSF has also been shown to activate stem cells and to be therapeutic in a mouse model of Parkinson's disease. Taurine and GCSF are additionally reported to prevent both apoptosis and ER stress-induced cell death in response to glutamate stimulation. Three model systems are currently in use to clarify the neuroprotective roles of GCSF and taurine: primary neuronal cultures, the rat stroke model, and the murine model of Parkinson's disease. Present results suggest inhibition of ER stress pathways by taurine in primary neuronal cultures subjected to hypoxia/re-oxygenation stress. Moreover, taurine seems to decrease H/R-induced cell death as measured by the ATP assay (Promega) as well as by TUNEL staining. Studies are underway to examine the effects of GCSF on inhibition of ER stress markers and on enhancement of neuronal cell survival. In addition, studies employing the MPTP Parkinson's model are in progress in order to determine the levels and localization of stem cell mobilization at 21 days after administration of GCSF. In the rat model of transitory brain ischemia, studies focus on the effect of prior GCSF administration on expression of ER stress markers and on decreasing infarct size at 2, 4, 7, 10, and 21 days following ischemia. Current data indicates a critical protective role for both taurine and GCSF against excitotoxic cell death, effective in both primary neurons as well as in in-vivo models: mouse Parkinson's model and rat transient brain ischemia model.

Student Researcher

Elizabeth Goldberger is a junior majoring in Chemistry who intends to attend medical school in the future. She is an active board member of the chemistry club and enjoys tutoring students at local public schools in New York City. In her spare time she enjoys singing as well as cooking and baking.
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Stem Cell Biology

Differential Expression of Lung Fractions as Determined by Quantitative PCR

by

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Lung disease affects millions of individuals worldwide, with current therapies providing limited benefits to most afflicted patients. Stem/progenitor cell therapies provide new hope to these patients, contributing to tissue regeneration by means of self-renewal and by multipotential differentiation into more diverse and specialized cell types. However, within the lung, the existence of adult stem cells to promote repair remains unclear.

The objective of the current research is to enrich for mouse lung alveolar epithelial type-2 cells that produce Surfactant Protein C (SPC), Clara cells that secrete Secretoglobin 1 (Scgbla1), and epithelial stem cells that are reported to co-express SPC and Scbgla1 proteins. Our method of choice is equilibrium density gradient centrifugation, which separates cells by buoyant properties. Experimentally, the lung was proteolytically digested and single cells were loaded onto a column composed of five discrete fractions that ranged from 1.00-1.08 g/mL. The column was centrifuged at 400 Rcf for 17 minutes, individual fractions were collected, and RNA was purified by the TRIzol™ method. Messenger RNA was then reverse transcribed by the Superscript II kit to complementary deoxyribose nucleic acid (cDNA). Quantitative real-time PCR was performed on mouse lung cDNA from separate fractions utilizing sequence-specific primers for SPC, Surfactant Protein B, Mucin 5, Aquaporin 5, CEBP alpha, and Scgbla1 transcripts. To determine relative mRNA transcript levels, threshold cycle (Ct) values were normalized to the housekeeping GAPDH gene with negative values indicating higher mRNA levels. Our results indicated that while only fractions 4 and 5 expressed CEBP alpha, fractions 3 and 5 were enriched for cells that express SPC and Scgbla1 genes. These data provide evidence that the buoyant density of lung epithelial and double positive epithelial progenitor cells range between 1.06-1.08 g/mL.

In summary, enrichment by density gradient centrifugation will help us understand pulmonary stem cells characteristics, compliment current methods used in stem cell purification, and contribute to the development of cell-based therapies of the lung.

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Student Researcher

Rebecca Tabaroki is a sophomore at Yeshiva University, majoring in Biology. In addition to being the Event Coordinator of Yeshiva University's Medical Ethics Society, Rebecca is passionate about continuing her education in the medical field, where she is interested in pursuing clinical research in addition to a career as a physician. In her spare time, Rebecca enjoys playing the piano, dancing, and spending time with her family and friends.

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Structural Biology

Effects on Phosphorylation by Receptor Tyrosine Kinase Deactivating Mutant

by

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Receptor tyrosine kinase (RTK) is a family of receptors expressed on the plasma membrane where it plays an essential role in cellular reproduction, specialization, and cell signaling. RTKs become activated when bound to their cognate extracellular growth-factor ligands, which, in most cases, facilitate RTK dimerization, auto-phosphorylation, and subsequent initiation of transduction pathways. When an RTK is in its inactive conformation, the tail of the kinase blocks the active site and inhibits the receptor's activation.

The short-term aim of this study was to determine how deactivation affects RTK phosphorylation. By transfecting cells with a deactivating RTK mutant, previously designed by our lab, we were able to observe changes in phosphorylation levels.

Spodoptera frugiperda Sf9 cells were harvested 33 hours after infection with the RTK gene construct deactivating mutant. Lysates were prepared and subjected to kinase buffer (containing ATP and $MgCl_2$). Western blotting was employed to assay for phosphorylation using anti-phosphotyrosine antibodies. Transfection of Sf9 cells with this gene construct revealed differential phosphorylation levels when treated with various reagents. These results provide an important basis with which to conduct further RTK activation studies in the future.

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BIU

YU-Bar-Ilan Summer Research Program

The Entire Opatowsky Lab

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Student Researcher

Dina Golfeiz is a graduating senior at Stern College majoring in Biology. She is interested in pursuing biomedical research as well as a career as a physician. When she is not playing with pipets in the lab, Dina enjoys drawing and reading in her free time.

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Biophysical Chemistry

Lipid Binding and Self-Aggregation of the Antimicrobial Peptide Daptomycin in Model Membrane Systems

by

Nancy Tishbi and Evan Mintzer

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Daptomycin (DAP, Figure 1) is a cyclic anti-microbial lipopeptide which is currently used for the treatment of infections caused by Gram-positive bacteria. DAP is comprised of a cyclic arrangement of standard and non-standard amino acids attached to a decanoyl fatty acid moiety N-linked to an exocyclic tryptophan residue. DAP's activity depends on the presence of calcium and is mediated by the depolarization of the target membrane. Results from a recent study by our collaborators provide evidence that DAP oligomerizes at the membrane level when calcium and membranes containing phosphatidylglycerol (PG) are present. In addition, they showed that oligomerization does not occur in the absence of membranes.

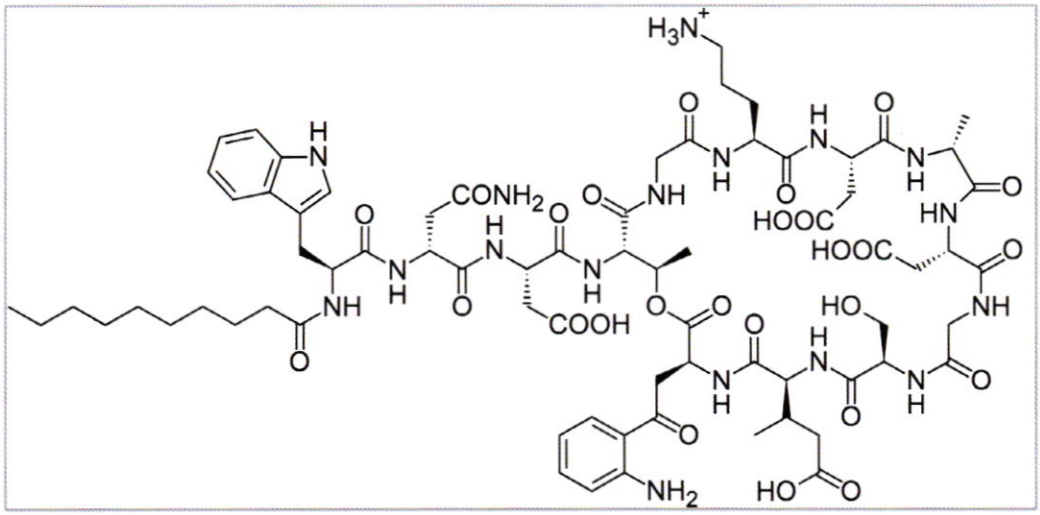

Figure 1. Molecular Strucutre of Daptomycin

Our goal with respect to this project is to obtain thermodynamic parameters for DAP-DAP and DAP-membrane interactions. Isothermal titration calorimetry (ITC) is a sensitive method used to obtain these parameters. By using ITC, the affinity of DAP for model membranes comprised of varied molar ratios of 1,2-dioleoyl-*sn*-glycero-3-phosphocholine (DOPG) and 1,2-dioleoyl-*sn*-glycero-3-phosphocholine (DOPC) were investigated.

For each ITC experiment, large unilamellar vesicle (LUV) suspensions of PC, PG, or various molar mixtures of these two lipids (5 mM total lipid) were prepared and injected into the reaction cell containing 23 μM DAP at 25°C. Both LUV and DAP solutions contained 1 mM calcium. Data obtained from these experiments were analyzed using Origin software. A sample isotherm and the associated integrated heats of binding are shown in Figure 2.

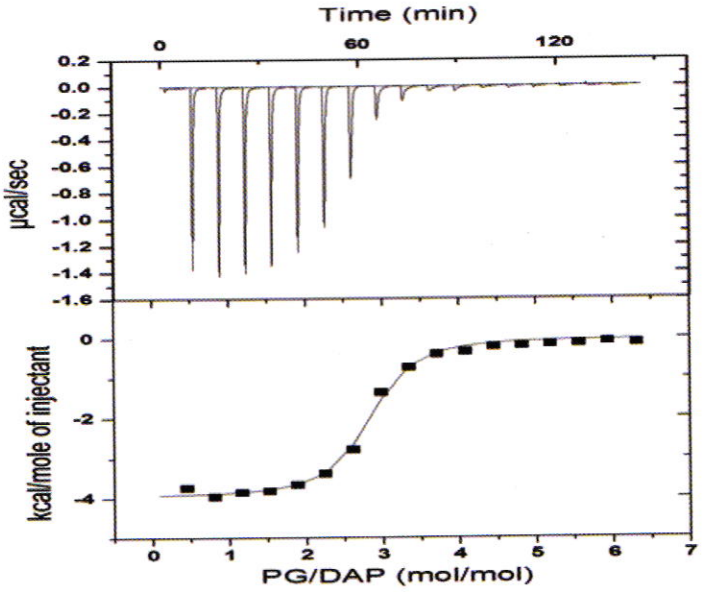

Figure 2. Top: Raw heats of binding from isothermal titration of 23 μM DAP with LUV comprised of DOPG/DOPC (60% PG, total lipid = 5 mM). Bottom: Integrated heats of binding. The points were fit using Origin's one-binding site model.

Thermodynamic parameters obtained in this set of experiments are summarized in Figure 3. These data show a clear trend in affinity of DAP for PG (K_d), G and H. The affinity increases as the ratio of PG/PC increases, illustrating a strong binding correlation between PG content and molecular binding. Interestingly, no binding was observed when DAP was titrated with pure PC or when calcium was replaced by magnesium (data not shown), illustrating the absolute requirement of DAP-membrane binding for PG and calcium.

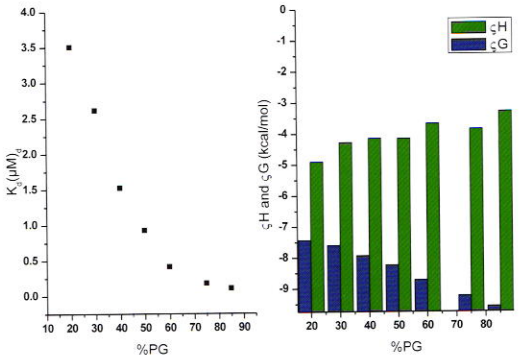

Figure 3. Summary of G and H (right panel) and dissociation constants (left panel) for DAP binding to PG/PC LUV of varying molar ratios.

Student Researcher
Nasim Tishbi is a junior at Stern College majoring in Biochemistry. Nasim came to the US with her family four years ago from Iran. Dedicated to the research world, as a YU Kressel Fellow, she has worked diligently in the biophysical chemistry lab of Dr. Evan Mintzer of Yeshiva University for the past two years. She would like to take this opportunity to thank Yeshiva University, the JFEW program and the Kressel Committee for supporting her in all of her academic work.
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Electrochemistry

Particle Size Distribution Studies of Cathode Materials for Li-Ion Batteries

by

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The Li-ion batteries that power many portable electronic devices generally consist of a graphite anode and a lithiated transition metal oxide cathode. The electrochemical activity of the battery, including the ability to charge quickly, is affected by properties of the cathode, such as the active surface area of the electrode material. This, in turn, generally correlates with the particle size of the electrode material. In order to obtain better electrochemical results, like higher rate capability, the particle size of the active material should be optimized, and the distribution of particle size uniform.

The particle size distribution of two cathode materials, Li_2MnO_3 and $xLi_2MnO_3(1\text{-}x)Li[Ni_aMn_bCo_c]O_2$, was studied using a MasterSizer 2000E device based on a laser diffraction method. For Li_2MnO_3, the particle size distribution of a ball-milled sample was compared to that of a control, pristine, sample (**Fig. 1, (1)**). The ball-milling was implemented for three hours at three-hundred rpm, using fifty spherical balls of five mm in diameter. The ball-milled Li_2MnO_3 was stirred for either two minutes (**Fig. 1, (2)**) or seven minutes (**Fig. 1, (3)**) before the measurement, and the particle size distributions were compared to that of the control. While the average diameter of the two ball-milled samples either increased from, or stayed the same as, that of the pristine (82.4 and 37.4 μm as compared to 37.3 μm), the distributions show particle sizes that are generally smaller from that of the pristine (Fig. 1). Stirring for seven minutes prior to the measurement decreased the amount of agglomerate particles of the ball-milled sample, allowing us to predict that a cathode constructed from vigorously stirred ball-milled active material should be more electrochemically active than the pristine. Electrochemical studies are currently underway to try to confirm this prediction.

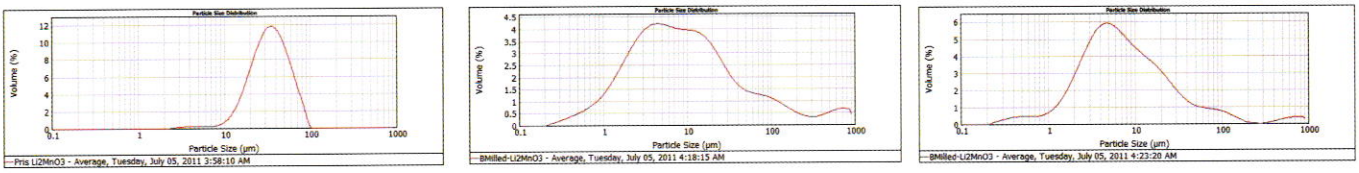

Figure 1. Logarithmic particle size distribution of Li_2MnO_3. From left: (1) Pristine, (2) Ball-milled - two minute stirring, (3) Ball-milled - seven minute stirring.

Two types of $xLi_2MnO_3(1\text{-}x)Li[Ni_aMn_bCo_c]O_2$ material were assessed, one with an active surface area of 0.6 m^2/g and one with a surface area of 7.0 m^2/g. While the electrochemical activity of the 7.0 m^2/g sample was much higher, the two samples had quite similar particle size distributions (and had similar average particle diameters of 22.4 and 22.2 μm respectively). The difference in surface

area and electrochemical activity was attributed, then, not to a difference in particle sizes, but (in part) to the porosity of the 7.0 m^2/g sample as compared to that of the 0.6 m^2/g sample. This difference was confirmed with analysis of SEM (Scanning Electron Microscope) images presented in **Figure 2.**

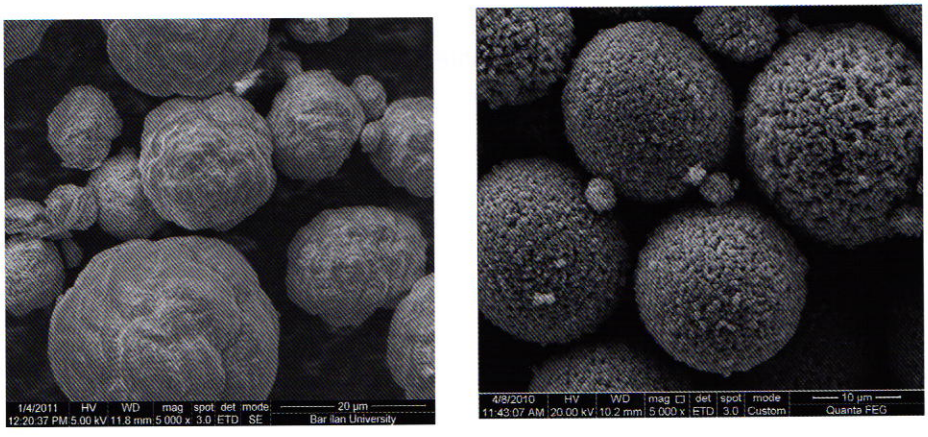

Figure 2. SEM images (5000x magnification) of $xLi_2MnO_3(1\text{-}x)Li[Ni_aMn_bCo_c]O_2$ cathode material. Left: Sample with specific surface area of 0.6 m^2/g; Non-Porous. Right: Sample with specific surface area of 7.0 m^2/g; Porous.

Student Researcher
Infused with Five Towns passion, Yair has a zeal for a random eclectic chulent of activities. He plays classical music on piano, enjoys rhetoric as an art, and is trying to pick up computer programming in his spare time — that is, when he isn't biking. His research focus spans from hydroxy-radical cleaved DNA footprints to computational basis-set limit extrapolations.

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Computational Chemistry

Molecular Dynamics Simulations of Ionic Liquids for CO_2 Capture

by

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The combustion of fossil fuels produces carbon dioxide, a potentially harmful product for the environment. A goal of "green-chemistry" is to be able to design an efficient way of capturing carbon dioxide from the post-combustion flue gas of power plants in order for the CO_2 to be recycled in an environmentally-friendly fashion.

Ionic Liquids (ILs), or low melting salts, display a very efficient ability of dissolving CO_2 due to the nature of their chemical makeup. Much research is currently being done on the properties of ILs in the hopes of being able to use these ILs to capture the large amounts of CO_2 produced by our power plants in the future.

Regarding Ionic Liquids, much research is being done in which the chemical properties of different Ionic Liquids are altered (different ion pairs, different atoms within each ion, etc...) and the effects to which these changes have on the ILs' abilities to dissolve CO_2 are analyzed. This research is needed because at the present time there are other problems associated with IL-CO_2 capture.

Molecular Dynamics simulations allow us to model many different systems of ILs and to analyze the different properties they exhibit in order to draw conclusions of how they might dissolve CO_2 on a molecular scale. Dr. Steven Corcelli's group at Notre Dame is researching the solvation properties of different ILs using time-correlation functions together with excitable probe molecules in order to gain a better understanding of the solvation dynamics of these Ionic Liquids. This understanding will help greatly in the goal of using ILs for the capture of CO_2 from post-combustion flue gas.

My research project involved carrying out simulations of Ionic Liquids using Molecular Dynamics simulations and to then write computer programs that analyzed the output data of the simulations for our specific purposes. My task was to gather certain chemical properties of simulated ILs and compare them to experimental results in order to verify the accuracy of our force field model. This verification step is necessary before proceeding to measure other simulated properties and to ultimately study the Ionic Liquid in question.

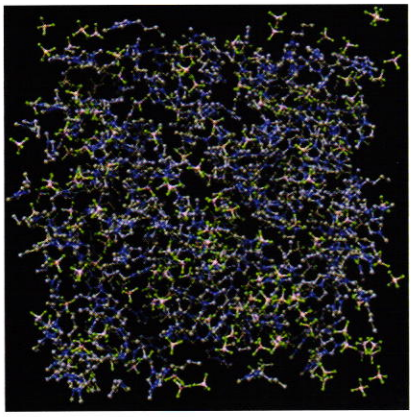

Figure 1. A snapshot from an initial phase of the equilibration process of a Molecular Dynamics simulation of a box of 512 molecules of the Ionic Liquid [Bmim][BF_4].

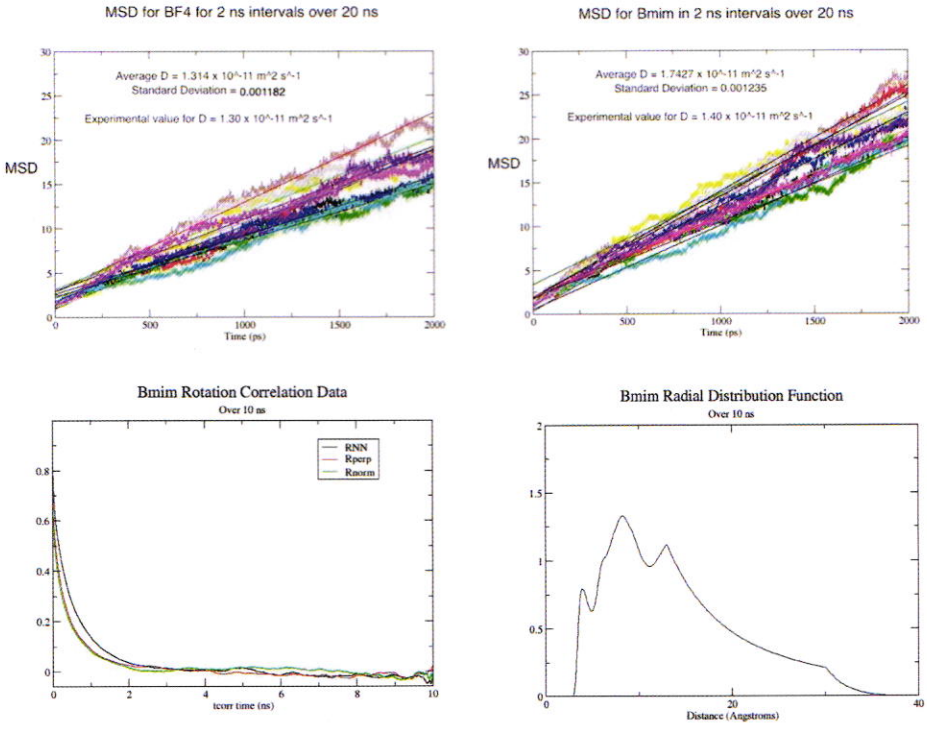

Figure 2. We have calculated the Diffusion constant as well as the Rotational Correlation Relaxtion Time of [Bmim][BF_4] via our simulation method and have verified that they compare accurately to experimental values. For example, the calculated Diffusion constants for [Bmim][BF_4] from simulation were $1.7x10^{-11}m^2s^{-1}$ and $1.3x10^{-11}m^2s^{-1}$ respectively. This compares quite well with experimental results of $1.4x10^{-11}m^2s^{-1}$ and $1.3x10^{-11}m^2s^{-1}$. Our simulated Rotational Relaxation Time for three atom vectors in our IL also reflect experimental trends. Thus, it is reasonable to assume that our simulation model accurately reflects real-life dynamics on the molecular scale for our particular Ionic Liquid. Also pictured above is the determined radial distribution function of [Bmim] molecules.

Student Researcher
Zachary Goldstein is a senior at Yeshiva College majoring in Chemistry. He is from South Bend, Indiana and will be applying to medical school this summer.
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Networking

Route Search in Mobile Ad-Hoc Networks

by

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In situations where communication is necessary but network infrastructure is unavailable, one viable solution is to set up a mobile ad-hoc network (MANET). Whereas in an infrastructure network, data is routed through preconfigured base stations, in an ad-hoc network each device itself acts as a router. In a MANET, data is sent from the source node to the destination node and will pass through intermediary nodes if the source and destination are not in direct transmission range.

Because of the highly mobile nature of the nodes in a MANET, reactive (on-demand) protocols are more suitable than proactive (table-driven) protocols. Rather than constantly updating a table of ideal paths between nodes which would require a very large-overhead and need to be constantly updated, the path between nodes is only determined (i.e. searched for) when it is requested.

The simplest way to obtain the shortest path is to flood the entire network. Under this approach, every node sends a route request to all of its neighbors. While this would succeed in finding the shortest path, it is impractical as it can lead to congestion and power consumption among other issues. Controlled flooding is therefore the preferred approach and over the past decade much research has been done in the areas of controlled flooding. Expanding Ring Search (ERS) is one form of controlled flooding in which each search for a path has an associated time- to-live (TTL) value. The search begins with a low TTL value and upon each unsuccessful search, the algorithm increases this value - thereby expanding the size of the ring that it searches. This continues until the destination is found or the entire network is flooded. Expanding Ring Search has been thoroughly researched and ideal sequences have been proposed such that ERS has a lower *expected* cost than uncontrolled flooding.

In all of the ERS research to date, the assumption has been that the entire search is taking place at a single point in time, and consequently the node locations do not change for the duration of the search. Our lab, however, is developing a new search algorithm that abandons this traditional assumption. Because the nodes are highly mobile, if we conducted an unsuccessful search, we need not necessarily raise the TTL value. Alternatively, we can wait some time and then repeat the search with the same TTL value. In order to prove the viability of this approach, we conduct simulation-based studies in which we show that the distribution of the nodes in the network can be learned. We use our knowledge of the distribution to demonstrate that when a small time delay is acceptable, Elastic Ring Search can be more efficient than Expanding Ring Search.

Student Researcher

Steven (Tzvi) Goldfeder is a graduating senior at Yeshiva College majoring in Computer Science and Mathematics. He conducted this research at Bar-Ilan University last summer as part of the YU Bar-Ilan Summer Science Research Program. He will continue studying Computer Science at Columbia University next fall.

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Risk Management

Risk Functions and the RISK Board Game

by

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Real-valued functions quantifying the risk of a decision or position have been used for a long time. For example, the variance and the expected utility of a random variable are of this type. Since the introduction of (monetary) risk measures in the influential paper, "Coherent Measures of Risk", Artzner et al. (1999), they have become a popular tool in risk measurement.

Risk measures tell us how risky a choice is, letting us decide if the risk is worth the reward. In this case, the choice is called acceptable. RISK, a game in which several decisions are made each turn, is a perfect forum for looking at how risk functions can help us make choices.

In this paper, we look at the question of how many units of armies must be added to make a situation acceptable, by using risk functions similar to Value at Risk. Since RISK only works with discrete numbers, the number of armies or the number of countries conquered, this game presents the challenge to deal with integer-valued risk measures rather than real-valued ones. In essence, our study will create a mathematical model of the game that can influence the decisions throughout each turn. Based on particular risk measures, risk units are assigned to trinomial trees, which model the battle for a given country. By doing so, we will be able to determine what types of situations we should be looking for while playing RISK. This is extremely different from earlier work that has been done on RISK, which has focused on how the probability of victory is impacted by an action. Instead, we look at more complex models in determining one's action. The final goal is to provide a framework such that computer programmers could create a computer opponent for RISK.

By examining RISK, we will also be able to further understand how decisions that involve risk can be made in the optimal fashion. In this way we are no longer examining just a game, but rather the decisions we make in the turns of our lives.

Student Researcher

A resident of Teaneck, NJ, Sam Reinstein is a forthcoming graduate of Yeshiva College's Honors program and is majoring in Mathematics while minoring in Business. He is interested in pursuing a career in the actuarial field. Sam will also be continuing his Judaic studies in RIETS to obtain ordination as a rabbi, while also obtaining a graduate degree in Jewish philosophy from the Bernard Revel School of Jewish Studies.

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Modeling the Volatility Smile

by

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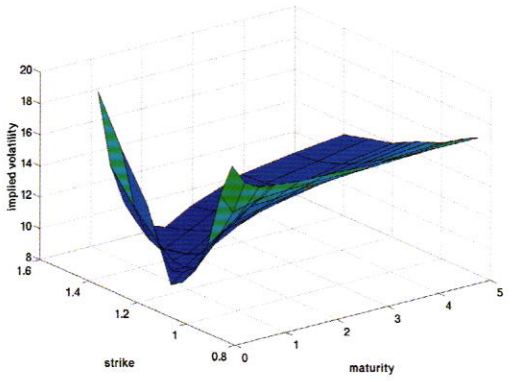
A financial market refers to any marketplace in which buyers and sellers participate in the trade of assets such as equities, bonds, currencies, and derivatives. A derivative is a financial contract whose value depends on underlying variables. An option is one type of derivative in which two parties propose a future transaction of an asset at a reference price. The buyer of the option has the right, but not the obligation, to activate that transaction, while the seller incurs the corresponding obligation to fulfill it. There are two types of options: call options and sell options, which give their holders the right to buy or sell, respectively, an underlying asset by a certain date for a certain price.

In mathematical finance, a "volatility smile" is a plot of the implied volatility of an option as a function of its strike price. The implied volatility is relatively low for at-the-money options and becomes progressively higher as option moves either into the money or out of the money. An older stochastic volatility model is the Black-Scholes model, which contains 5 parameters: the current price, the strike price, the interest rate, the expiration, and the volatility. The newer SABR model below attempts to capture the volatility smile in derivative markets [1].



Unlike the Black-Scholes model, the SABR model assumes that volatility varies erratically. With this assumption and various corrections made by Jan Oblo [2] to the model, we altered previous models to better imitate the Smile. Using Matlab, we optimized the parameters and graphed 3 different strike prices using this SABR model. We then used various macros and functions in Excel to evaluate the desirability of an option. Such a model for desirability, if proven accurate, would be highly attractive to those in the financial field.

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[1]*University of Trier – Department of Mathematics. April 18 2012 < http://www.math.uni-trier.de/~sachs/scientific_interests/projects/heston_calibration.htm >*

[2]*Jan Obloj, Fine-tune your smile: Correction to Hagan et al, arXiv:0708.0998v3 [q-fin.CP].*

This research was conducted as part of the Yeshiva University - Bar Ilan Summer Research Program.

Student Researcher

Sam Cohen is a third year Mathematics and Pre-engineering Major with a focus in computer science. Sam is the captain of the Yeshiva Cross-Country (XC) team, and led his team to a 2nd consecutive victory at the HVMACs championship race. He is also involved in Yeshiva College Dramatics Society (YCDS), as he greatly enjoys the arts. Hailing from Toronto, Sam hopes to be drafted by the Maple Leafs at some point next year.

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Quantum Mechanics

New Families of Coherent States for the Supersymmetric Oscillator

by

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Supersymmetry is a viable theoretical framework to provide a unified picture of fermionic and bosonic fields. The subjacent supersymmetric algebra intrinsically transforms bosonic degrees of freedom into fermionic ones and vice-versa. Aside from physical realizations, the mathematical objects of supersymmetry (e.g. superspace, supertransformations) have proved fruitful for solving quantum problems based on the concept of partner Hamiltonians. The harmonic oscillator has been extensively studied in this context; a result of particular interest is the vanishing zero-point energy. The supercoherent states were first introduced 25 years ago [1], defined as eigenstates of a generalized annihilation operator that mixes fermionic and bosonic degrees of freedom. Here we extend that original annihilation operator to a family of complex 3-parameter annihilation operators. Our presentation shows the properties of those new operators as well as the properties of the corresponding eigenstates. In particular, after explicitly calculating the eigenstates in parameter space, we present a subspace with bounded uncertainty, for both the Heisenberg and entropic formulations of uncertainty.

[1] Supercoherent States, C. Aragone and F. Zypman, Published in J. Phys. A 2267 (1986)

Student Researcher

Mordechai Kornbluth is a fourth-year student at Yeshiva College pursuing an Honors degree, with a major in Physics and minors in Mathematics and (just for fun) Semitic Languages. In his monotonically decreasing spare time, he enjoys intellectual pursuits such as physics research and rigorous Talmud analysis, as well as listening to classical music. After he completes his undergraduate education, he intends to spend even more time in school in pursuit of a Ph.D., followed by a career in research.
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Nanoscience

Thermodynamic Properties of Nanoporous Gold

by

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Nanoporous Gold (NPG) is known to exhibit different catalytic properties from bulk gold. In contrast to the inert nature of bulk Au, NPG can reduce oxygen to both hydrogen peroxide and water. In addition, NPG is a 'green catalyst,' exhibiting high catalytic efficiency under relatively low temperatures. The pores of NPG are created through chemically extracting Ag from an alloy composed of Au and Ag. Our experiment used Extended X-ray Absorption Fine Structure (EXAFS) to determine the local atomic structure of NPG in order to study the influence of NPG's porous surface on its enhanced catalytic reactivity. We studied samples of NPG and the original Au-Ag alloys on Au and Ag x-ray absorption edges, independently. The size of the pores in our NPG samples ranged from 15 to 50 nm.

In EXAFS, interfering photoelectron waves are created through bombarding NPG with x-rays of sufficient energy to excite its core shell electrons. As an ejected photoelectron wave scatters from the atoms around the absorbing atom, it creates interferences between the outgoing and scattered parts of the photoelectron wave-function. This behaviour causes an energy-dependent variation in the x-ray absorption probability, which is proportional to the x-ray absorption coefficient. These modulations provide information about the structure, atomic number, structural disorder, and thermal motions of neighbouring atoms.

In our experiment, physical and thermal properties such as the coordination number (N), structural disorder (σ^2), nearest-neighbour atomic distance (R), Thermal Expansion Coefficient and Einstein Temperature were obtained. The EXAFS measurements were carried out at set temperatures ranging from 673 K to approximately 183 K. We calibrated the instrument using bulk Au and Ag samples, and our Einstein and Debye temperatures exhibited good agreement with other recorded literature values.

Our experimental data indicated that the nearest neighbor distances of the Au-Au bonds in NPG were reduced by ca. 0.01 Å compared to the bulk. We attributed this reduction to the surface tension in NPG, caused by the finite size effect of the NPG ligaments. The surface to volume fraction of Au atoms was also responsible for our observed reduction of NPG's Debye temperature by 5%, compared with the bulk.

Kästle et al[1] proposed that the phonon spectrum of gold thin films is really a superposition of the bulk and the surface spectra, weighted with the surface-to-volume fraction of Au atoms. Using this model, we were able to estimate that the surface bonds (with the reduced Debye temperature) extend within 4 layers of Au atoms located on NPG's surface.

Our findings indicated that the properties of NPG are affected by the sizes of NPG ligaments. The ligament dimensions may influence both the Au-Au distance reduction, and the surface-to-volume fraction of the first 4 layers of Au atoms on the NPG surface. Therefore, our results may offer a possibility to rationally design NPG with desired thermodynamic properties, through varying the de-alloying time.[2] In addition, one may also control the static and dynamic bond length disorder through varying the annealing time and the strain in thin NPG films. Further studies are required to confirm such capabilities, and they are presently in progress.

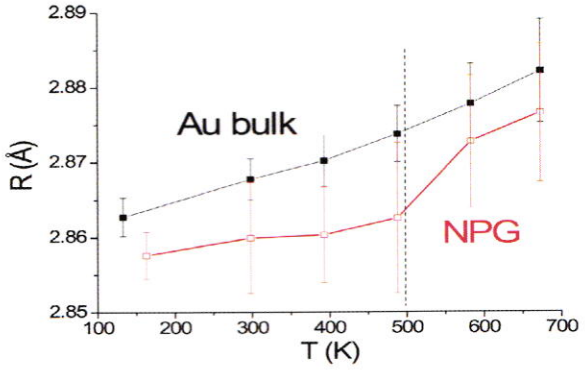

Figure 1. Au-Au distances in the bulk Au and NPG. Vertical line indicates the temperature at which NPG coarsens.

Table 1. Numerical results of the Einstein and Debye temperatures and linear thermal expansion coefficients, obtained by EXAFS analysis in bulk Au, bulk Ag and NPG.

	U_E (K)	U_D (K)	α (K^{-1}) ($\times 10^5$)
Au bulk	143(1)	182(2)	1.4(1)
Ag bulk	178(2)	226(3)	1.5(2)
NPG	137(2)	174(2)	1.0(4)

We appreciate the support of the Catalysis Center for Energy Innovations by the University of Delaware, and the travel support by the Synchrotron Catalysis Consortium.

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Student Researcher

Bluma Dukesz completed a B.A. in Chemistry at Stern College for Women in 2012. She plans to begin her graduate studies at the SUNY College of Optometry this fall. She was the recipient of a Summer Research Fellowship by the Catalysis Center for Energy Innovations at the University of Delaware (2011).

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Behavioral Neuroendocrinology

Effects of Endogenous and Exogenous Sex Hormones on Object Memory and Spatial Ability in Young and Aged Women

by

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The goal of the present study was to determine whether object memory and spatial ability decline with age in women and to examine hormone effects on object memory and spatial ability in young and aged women. Young women taking hormone birth control (HBC) were compared to young women not taking HBC. Young women who were menstruating were also compared to young women who were not menstruating during the time of testing. Exogenous hormone use in aged women was examined by comparing those taking prescription hormone therapy (HT) to those not taking HT. Results suggest that there is age-related cognitive decline in object memory and spatial ability in women. Further, HT impaired object memory, but enhanced spatial ability in aged women. In young women, neither HBC nor time of menstruation had significant effects on object memory or spatial ability.

Student Researcher

Malka Zughaft is a senior at Stern College majoring in Psychology. She is currently managing Dr. Lauren Harburger's research laboratory at Stern College and is assisting with her research studies. Malka aspires to continue her learning in graduate school and obtain a Ph.D. in Clinical Neuropsychology with an emphasis in Health.

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Social Psychology

Second Generation Holocaust Survivors

by

Mollie Lindell[1], Bea Hollander-Goldfein[2], Nancy Isserman[2], and Judy Levin[2]

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A trauma can be so severe that its impact is felt across generations. The trauma caused by the devastating and demoralizing war against the Jews known as the Holocaust is one such example. The extent to which the horrific trauma experienced by survivors has impacted the next generation requires much investigation. Second generation Holocaust survivors, although they did not experience the Holocaust, may feel traumatized from its physical and emotional brutality. Despite the fact that the brutality was inflicted solely upon their parents, children of survivors may feel its impact in a very tangible way. Their parents may have parented in a way that reflected their inner pain, oscillating between loving and caring for their children and languishing in their memories of the past.

The question of whether this inner pain caused by the trauma was indeed transmitted through the generations is subject to much debate. Nonclinical studies usually do not find any difference between second generation Holocaust survivors and comparison groups. However, most clinically-based studies find that children of survivors suffer from this trauma. These studies often point to the parents' unresolved mourning of the trauma, which prompted their irregular parenting styles and helped form disorganized attachment styles in their children. Parents also tended to keep their Holocaust experiences secret from their children, hoping to shield them from the horrors, which could impede their normal development, but the children found it difficult to relate to their parents without a more complete knowledge of their parents' life experiences. Because some survivors keep silent about the Holocaust, their children digest the nonverbal communication about it without quite understanding the mixed messages that were unintentionally sent. Whether through nonverbal communication or through genetic predisposition, "survivor guilt," irrational remorse for having outlived loved ones, seems to have been transmitted to the next generation. Children of survivors feel guilty that their parents are suffering, even though they are entirely blameless, and this susceptibility to feeling the same way as their parents points to the conclusion that trauma from the Holocaust is, indeed, transmitted to the next generation.

To resolve the debate of whether transmission of trauma to the next generation exists, the Transcending Trauma Project originated the idea that all impacts of the Holocaust, from survivor resiliency to transmission of trauma, are based on a continuum. Some second generation Holocaust survivors are traumatized from vicariously enduring the Holocaust, and others are unscathed. Some are traumatized in one aspect of their lives and function normally within other realms. The outcome essentially depends on how the survivors conduct their significant relationships.

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Student Researcher

Mollie Lindell is a Psychology major at Stern College for Women. In the summer of 2011, Mollie worked for Bea Hollander-Goldfein on Holocaust trauma research at the Council for Relationship's *Transcending Trauma* project in Philadelphia, PA.

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Clinical Neuroscience

Multisensory Processing In Children with Autism

by

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Viewing a person's articulatory movements substantially improves a listener's ability to understand spoken words, especially under noisy environmental conditions. A prominent theory in autism proposes that automatic multisensory integration (MSI) is impaired in this population, thereby inhibiting effective perception. However, direct empirical support of such deficits remains scarce. Impairment in communication is one of the hallmark symptoms in autism and the ability to perceive speech is a fundamental prerequisite for communication.

In our study, we assessed whether the integration of auditory and visual speech signals is impaired in high functioning children with ASD, by presenting them with monosyllabic words in auditory alone, audiovisual (AV) and visual (V) alone conditions, under varying signal-to-noise ratios. If MSI is indeed impaired in persons with autism, results signifying reduced gain in AV Integration would be expected. A large deficit in the ability of ASD children (ages 7-12) to integrate information from two senses was indeed expressed, as reduced AV gain, while performance in the auditory alone conditions was relatively normal. However, surprisingly, ASD children, ages 13-17, exhibited comparable AV gain with TD teens, implying a recovery of MSI in the teenage years. This finding provides hope for parents of ASD children that, assuming no mechanism is inherently broken, early intervention may drastically reduce the MSI deficit exhibited by younger ASD children. Differences in how multisensory inputs are integrated, and how these differences affect higher-order processing, as well as the impact of early intervention on the pathogenesis of persons with ASD, remain to be explored.

Acknowledgements

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Student Researcher

Miriam Steinberger is a senior at Stern College majoring in Biology. With plans to pursue a career in medicine, Miriam aspires to help others navigate difficult life situations. Aside from participating in biomedical research, she enjoys dancing, swimming and going to interesting speeches.

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Public Health

Optimizing Pediatric Rheumatology Training of Adult Rheumatology Fellows

by

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Purpose: The approximately 250 board certified Pediatric Rheumatologists in the United States are unable to see all of the children in need of specialized rheumatologic care. Consequently, many pediatric patients receive this care from practitioners trained in internal medicine and/or adult rheumatology. With only 10-20 fellows graduating from pediatric rheumatology training programs each year, reliance on non-pediatricians is likely to continue for the foreseeable future. Little is known about how best to prepare adult-trained providers to care for children. We examined the views of adult rheumatology fellows (ARF) training in a pediatric rheumatology clinic in an attempt to learn how to optimize a pediatric training program for adult rheumatologists.

Methods: Three to six ARF have received weekly pediatric rheumatology training at our institution annually since 2005. ARF were surveyed at the start and end of their 3-month pediatric rotation in an attempt to gauge their overall comfort level treating pediatric patients. Further survey items focused on identifying specific aspects of pediatric care viewed as most dissimilar from adult medicine, and diagnoses about which the ARF most wanted to learn. Follow-up questionnaires asked for rank ordering of major strengths and weaknesses of the pediatric rheumatology training. Visual analog and ordinal scales were utilized, and respondents were asked to elaborate on their answers using unstructured specification.

Results: Initially, adult rheumatology fellows reported low comfort levels treating pediatric patients, with a median score of 25 on a 100 mm visual analog scale ranging from utterly uncomfortable seeing children to completely comfortable with my ability to assess children. Upon completion of the 3-month long pediatric rotation, comfort levels rose to a median of 75 on the 100 mm scale. The value of the pediatric rheumatology experience was given a median ranking of 93 on a 100 mm VAS ranging from complete waste of time to outstanding experience. The aspect of care that was reported to be most different between pediatric and adult medicine before the rotation was growth and development issues, with all currently processed responses ranking it as such. The diagnoses unique to children about which fellows most wanted to learn were, in order, juvenile arthritis, SLE, and Kawasaki disease. Responses were positively correlated with the incidence of the condition.

Conclusion: This is a preliminary report of an ongoing prospective analysis of adult rheumatology fellows' training in pediatric rheumatology. Results support an apparent efficacy of rotations in pediatric rheumatology to prepare ARF for the care of pediatric patients. Data concerning particular areas of interest and perceived need are being identified. Analysis remains incomplete and numbers analyzed to date are small. Ongoing data analysis, as well as comparison of subjective responses with objective measures of performance, may identify specific approaches that could optimize training of ARF.

Disclosure: Eliezer Mendelev: None; Robert P. Sundel: None.

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Student Researcher

Eliezer Mendelev is a sophomore majoring in Biology and minoring in Public Health. He aspires to become a practicing physician in addition to pursuing clinical research. Eliezer's research interests include healthcare optimization and the reduction of preventable deaths. In his spare time, he enjoys photography and cooking.

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Public Health

Challenges to Efficient Delivery of Respiratory-Gated Radiotherapy: Patient and Staff Perspectives

by

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Purpose: Stereotactic body radiotherapy is a valuable treatment for upper abdominal malignancies. Respiratory motion, however, affects all tumor sites in the thorax and abdomen. Respiratory-gated radiotherapy (RGRT) is a method to limit the deleterious effects of respiratory motion during radiation delivery. Respiratory gating software requires that the patient maintain a constant, rhythmic breathing pattern. Disruptions in this pattern lead to an increase in treatment time, anxiety and physical discomfort, and decreased efficacy of treatment. We sought to identify the primary challenges to treatment deliveryv in order to inform the development of interventions to address these challenges.

Methods and Materials: We conducted structured interviews to assess patient physical and psychological discomfort during RGRT, as well as to evaluate staff perspectives on challenges to treatment delivery. A convenience sample consisted of 20 participants (10 patients undergoing RGRT for abdominal malignancies and 10 staff members – radiation oncology technicians involved in treatment delivery).

Results: The majority of patients reported physical pain or discomfort (70%) and falling asleep (60%) as their greatest challenges during the procedure. Breathing dysregulation was reported as a challenge by one third of patients. Anxiety, claustrophobia, restlessness and boredom were reported infrequently. Consistent with these findings, staff members reported physical pain or discomfort (70%) and falling asleep (80%) as two of the greatest challenges to treatment delivery. Additionally, 50% of staff reported anxiety and restlessness as challenges.

Conclusion: Our findings indicate that physical pain or discomfort and falling asleep, both of which adversely impact the consistent breathing pattern required during the procedure, are the greatest challenges to effective delivery of RGRT. Additional challenges include anxiety and restlessness. Based on these results, a mindfulness-meditation-based psychosocial intervention will be developed to help patients cope with physical pain or discomfort and maintain the appropriate level of wakefulness during RGRT treatment.

Student Researcher

Michael Epstein is a senior at Yeshiva College completing a major in Biology. Upon graduation, Michael plans to enter dental school. Michael is particularly interested in alternative medicine cancer research and in his free time, he enjoys cooking.

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Public Health

Clinical Outcomes of Delirium in Elderly Patients Admitted From the Emergency Department & Quality Assurance Evaluation of Delirium in Patients in the MICU, SICU, and CSICU

by

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Objectives:
(1) To measure the prevalence of delirium and its psychomotor subtypes in Emergency Department patient greater than or equal to 65 years of age who are admitted to the hospital inpatient wards.
(2) To test the association between delirium and subsequent morbidity and mortality after admission.
(3) To evaluate the prevalence of delirium in the medical intensive care unit (ICU), the surgical ICU, and the cardiothoracic ICU.

Background:
Delirium has been defined as a syndrome involving acute alterations in mental status with a fluctuating course and inattention [1]. In older patients, delirium has been associated with multiple negative consequences, including increased mortality, hospitalization, increased costs of care, and greater risk for cognitive decline [2, 3]. In the Emergency Department (ED) as many as 8% of older patients may have delirium and 76% of these cases may be missed by ED physicians [4]. However, previous studies have not analyzed the association between of delirium in older ED patients and subsequent inpatient outcomes. This study aims to analyze the hypothesis that patients diagnosed with delirium at the time of admission from the ED will present with worsening outcomes and increased mortality and morbidity. The determination of such a correlation would allow for the implementation of earlier delirium interventions both in the ED and the inpatient wards.

Methods:
Approval for the study protocol was provided by the Einstein-Montefiore institutional review board. Our study involves a prospective observational cohort of 200 elderly patients. Inclusion criteria for the study were patients in the Emergency Department, of an age equal to or greater than 65 years, with planned admission to the Moses or Weiler divisions of Montefiore Medical Center. Patients were excluded for being non-English speaking, refusing consent or having a surrogate refuse consent, having an altered mental status and no surrogate to consent for them, being admitted to the medical ICU, surgical ICU, cardiothoracic ICU, or critical care units, having psychiatric illness, being in a comatose state, or suffering from severe dementia or neurocognitive disease at baseline such that the patient was nonverbal or unable to follow basic commands (mild to moderate dementia was not excluded). Patients were enrolled while in the ED through an oral consent performed by a research assistant.

Research assistants assessed the patient level of consciousness in the ED and determined the delirium status of the patient through the CAM-ICU protocol [5]. The CAM-ICU involves a short two minute assessment of inattention, disorganized thinking, and altered level of consciousness. CAM-ICU assessment was performed on the first day in the ED and over the subsequent two days during the patients in-patient stay until hospital day three. If a patient was determined to not be delirious, research assistants performed an assessment of cognitive functional status by employing the Memory Impairment Screen (MIS) and a Katz Activities of Daily Living assessment [6, 7]. Additional data was also collected from non-delirious patients regarding occupational status, educational levels, and leisure activities. For delirious patients a shortened Informant Questionnaire on Cognitive Decline

(IQCODE) for the elderly was administered to a healthcare surrogate along with the Katz and other baselines assessments. The MIS or IQCODE and Katz were performed on the same day.

Over the course of the study medical records were analyzed to collect ED laboratory data and vitals and inpatient medical history, consultations, and other outcomes. Data was collected through 28 days or until hospital discharge. All patient data was made anonymous through assignment of a unique study number and electronically secured behind password protected databases. Any identifying information is to be destroyed at the conclusion of the study.

Results and Conclusions

Both the clinical study and the quality assurance project are ongoing and no definitive results have been obtained. Currently 501 patients have been screened for the study and 67 patients have been recruited (Figure 1). Of the 67 recruited patients 5 were CAM positive for one day during the three day screening period and 62 were CAM negative for every day within the three day screening period. We project the trial recruitment to be complete within the next two to three months.

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Student Researchers

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Channah Esan is junior at Stern College for Women majoring in neurobiology with hopes of pursuing a career as a neuroanatomist. She is active on campus as the president of pre-med club, a peer tutor, resident advisor, and proud member of the soccer team. Go lady Macs!
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Koral Dadon is currently a junior at Stern College, with a majoring in Biology and a minor in Chemistry. Her research at Montefiore Medical Center clarified her aspiration to become a doctor. She plans to continue her education in the medical field, where she's interested in becoming a gynecologist.
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